Benign Anorectal Disorders

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A thesis submitted to the University of New South Wales for the Degree of Doctor of Medicine

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ABSTRACT

Problem Investigated:
A multitude of benign disorders affect the anorectal complex often resulting in significant morbidity. For many of these conditions the pathophysiology and clinical management continue to be debated. This is particularly so for anal fissures, anal incontinence and pelvic floor dysfunction.

Procedures Followed:
A series of clinical trials was performed.

Anal Fissure: Two current management regimes for chronic anal fissure, Glyceryl Trinitrate and Botulinum Toxin, were prospectively assessed for manometric and clinical outcome. A new treatment regime, inducible nitric oxide, was prospectively assessed in an animal model and a new manometric observation in anal fissure patients, the Fast Wave, was validated.

Anal Incontinence: The magnitude of the problem and the relative role of several previously identified risk factors was assessed from a manometric database. The impact of a standard treatment for Crohn’s disease, the seton, on anal continence was assessed via a retrospective cohort study. The long-term outcome of dynamic graciloplasty and re-do anal sphincter repair, two previously accepted treatments for anal incontinence, were also assessed retrospectively. A new intervention for treating anal incontinence, the magnetic ‘Chair’, was prospectively trialed in incontinent patients.

Pelvic Floor Dysfunction: A new treatment option for rectocele, the laparoscopic repair, was compared with an accepted treatment option, the transanal repair via a matched cohort study. A further group of patients with multiple symptoms of pelvic floor dysfunction undergoing the same laparoscopic technique were then prospectively assessed for functional outcome across the pelvic floor compartments.
General Results:

Anal Fissure; The manometric effects of both glyceryl trinitrate and botulinum toxin, demonstrated in this thesis would imply that their mode of impact on the anal sphincter is other than that of anal pressure reduction. Fissure healing is dependent upon the pre-treatment anal resting pressure and fissure grade, not anal pressures following treatment. Inducible nitric oxide does not increase nitrate levels in the rat internal anal sphincter. A new manometric wave form in the hypertonic internal anal sphincter, the Fast Wave, has been validated.

Faecal Incontinence; Faecal incontinence is multi-factorial. However, obstetric birth injuries are the most significant factor predisposing to faecal incontinence following age. Furthermore current government policies are failing to address the problem. The dynamic graciloplasty provides symptomatic long-term relief in only 16 percent of patients and results in significant co-morbidity in most patients. Re-do anal sphincter repair provides relief in 60 percent of patients without further side effects. The use of a seton in Crohn’s perianal disease prevents deterioration of patient continence. Extracorporeal magnetic stimulation, the Chair, may provide significant relief for patients with faecal incontinence.

Pelvic Floor Dysfunction: The laparoscopic posterior compartment repair provides relief of bowel symptoms in 31 percent of patients. This does not compare favourably with the transanal long-term symptomatic improvement of 67 percent. The results of the laparoscopic pelvic floor repair in patients with multiple symptoms of pelvic floor dysfunction is disappointing, particularly for bowel and bladder symptom improvement.

Major Conclusions: This thesis questions the accepted pathophysiology of anal fissure, highlights the long-term implications of obstetric childbirth injuries on faecal continence and raises concerns about current management strategies for faecal incontinence and pelvic floor dysfunction.
STATEMENT

I hereby declare that his submission is my own work and to the best of my knowledge it contains no material previously published or written by another person, nor material which to a substantial extent has been accepted for the award of any other degree or diploma at UNSW or any other educational institution, except where due acknowledgement is made in the thesis. Any contribution made to the research of others with whom I have worked at UNSW or elsewhere, is explicitly acknowledged in the thesis.

I also declare that the intellectual content of this thesis is the product of my own work, except to the extent that assistance from others in the project’s design and conception or in style, presentation and linguistic expression is acknowledged.

I also declare that disposition of the thesis with the University of New South Wales is in accordance with the University’s Policy with respect to the Use of Project Reports and Higher Degree Theses.

Michelle Thornton
ACKNOWLEDGEMENTS

I was introduced to this fascinating area of research by Professors Denis King and David Lubowski. I am grateful to both for the level of support and encouragement they provided throughout my research and subsequent compilation of this thesis. To Professor King I also owe my thanks for providing the avenue through which this thesis became a reality. I would also like to thank Professor David Morris for his co-supervision and academic advice. My gratitude also extends to Michael Kennedy and the members of the Pelvic Floor Unit at St George Hospital for their ongoing support and good humour.

At a technical level, chapter 2.3 was supported greatly by the efforts of Professor King, Dr Yasemin Baldik. The manometric aspects of Chapters 2.1, 2.2 and 3.5 were greatly supported by Michael Kennedy. My thanks is owed to Professor Alan Lam for access to his pelvic dysfunction patients for the purpose of chapter 4.

I would also like to acknowledge my debt to the Sydney Colorectal Associates and Mr Harry Triguboff. Without the benefit of their Harry Triguboff research scholarship (2003) the period of study would have been considerably more arduous.

Finally, I would like to thank Mr Kevin Robertson. His support, tolerance and encouragement throughout the thesis period was invaluable.
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CHAPTER 1

INTRODUCTION
**Benign Anorectal Disorders**

**Introduction**

The benign conditions investigated in the following chapters are the result of anatomical or physiological dysfunction. A basic understanding of normal anorectal structure and function is therefore paramount to understanding the conditions and treatment modalities investigated. The currently accepted hypotheses are given below. As will be evident, much controversy still exists over what would seem basic structure and function.

**Functional Anatomy and Physiology**

The anal canal, the upper limit of which is the anorectal junction, begins at the anal verge and is 1.5-4.0cm in length. The anal canal is lined by squamous through to columnar epithelium with a rich parasympathetic sensory innervation (S2,3,4). This area is responsible for rectal sampling, whereby a reflex and conscious decision can be made about the need for defaecation. The anal canal is also the site of the haemorrhoidal complex, or anal cushions, which are important for the maintenance of anal continence, contributing up to 20% of resting anal pressure (Sangwan 1998).

Although the anorectum has a potential dual blood supply from the inferior and middle rectal arteries, there are no intramural collaterals between the branches of the inferior rectal artery in the anal canal. This combined with the vascular pathway through the internal sphincter creates an area of potential midline ischaemia (Klosterhalfen 1982).

The other structures within the length of the anal canal essential to the disease processes investigated are the anal sphincters, internal and external.

**Internal anal sphincter (IAS)**

The IAS is the thickened downward extension of the rectum, the inner, involuntary, smooth muscle component of the anal sphincter complex. The maintenance of anal tone at rest is attributed to the internal anal sphincter,
providing at least 60% of the resting anal pressure (Bennett 1964, Gutierrez 1975). Excitatory IAS activity is thought to be mediated by a tonic alpha-1 adrenoceptor sympathetic discharge (Parks 1966, Friedman 1968, Speakman 1997), with low amplitude waves, slow waves, occurring at a frequency of 10-20 per minute. Less frequently, ultra-slow waves, occurring at a frequency of two per minute are observed (Hancock 1976). The significance of this wave activity is poorly understood. However, both are displayed in isolated strips of IAS and it is hypothesised that they are responsible for maintaining continence in the presence of increasing rectal pressure waves. Nitric Oxide (NO) is thought to be the principle nonadrenergic, noncholinergic neurotransmitter in the IAS and its release results in IAS relaxation (O’Kelly 1993, Rattan 1992). Internal anal sphincter relaxation also occurs as part of the recto-anal inhibitory reflex (RAIR). The pathways involved in the mediation of this reflex have been the subject of much debate. However, ablation of the reflex in circumferential myotomy (Lubowski 1987) and the identification of shunt fascicles, a rapid means of two-way transfer of neuronal information between rectum and sigmoid colon, in the rectum in humans (Kumar 1989), indicates an intramural process. Blockage or the RAIR with topical anaesthesia suggests that the receptors for the RAIR are located in the rectal mucosa (Gaston 1948). Adenosine triphosphate was hypothesized to be the mediator (Sanders 1992) but recent studies suggest that alpha-2-adrenoceptors are responsible (Speakman 1997). However, the level at which these receptors modulate the internal anal sphincter relaxation is not clear, particularly in light of more recent research which did not identify sympathetic ganglia in the internal anal sphincter (Jones 2003, Jones 2004).

External Anal Sphincter (EAS)

The anatomy of the EAS is the subject of continuing debate. The traditional concept of the EAS was three concentric muscles that contracted en-mass (Milligan 1934). Goligher demonstrated that the muscle was one continuous sheet rather than three separate muscles (Goligher 1949). Shafik then suggested that the EAS is three counterpoised, U-shaped loops and that contrary to the belief that continence is the results of squeezing.
circumferentially, it was suggested that continence is maintained by kinking the anal canal in contrary directions (Shafik 1975). More recently it has again been suggested that the EAS is one muscle, the deepest part being intimately related to the puborectalis muscle which is integral to both levator ani and EAS muscle complexes (Ayoub 1979).

The EAS is innervated by the inferior rectal nerve, a branch of the pudendal nerves (S2-4). The EAS reflexly contracts at the time of IAS relaxation to maintain continence during rectal sampling. Voluntary contraction of the EAS can extend the period of continence and allow time for compliance mechanisms within the colon to compensate for the increased intrarectal volume. External anal sphincter contraction is responsible for the voluntary squeeze and cough pressure measured with anorectal manometry.

**Anorectal Manometry**

Anorectal manometry provides objective data about the components of the sphincter complex (Lubowski 1999). There is no standardised conduct of anal manometry. The techniques applied in this thesis assessed functional sphincter integrity with a stationary water perfused manometric catheter. A six-channel, low compliance, side-hole, water perfusion system with computer acquisition and storage of data (Neomedix, Sydney, Australia) was used to measure resting, squeeze and anal cough pressures. The most caudal recording port was positioned in the lower anal canal, so that five channels 0.75cm apart recorded anal canal pressure, and one (or more if the anal canal was short) recorded rectal pressure. Anal pressures were measured once a stable baseline was established.

Although the reliability of anorectal manometry has been questioned, it is currently the most accessible and tolerated assessment of anorectal function (Ryhammer 1997). All our investigations were performed firstly in the left lateral position. Those patients studied in Chapter 3.4 were also investigated sitting in a chair. We specifically chose stationary anorectal manometry. The pull-through technique used in some earlier studies (Brisinda 1999) has been
shown to stimulate the internal anal sphincter, artificially raising RAP (Rao 1999, Sun 1989). Furthermore, our experience is that patient distraction with catheter movement or involvement in conversation can impact on the RAP. While maintenance of a stationary environment may be criticised as not reflecting normal activity, this method allowed result comparison across the groups to assess inter-observer variability. Anorectal physiology was performed by two assessors [MT, MK]. Eighty-three percent of patients across all study groups were investigated by both assessors. A student t-test comparing the maximum resting pressure of individual patients as assessed by both assessors, confirmed the absence of inter-observer variability. Ninety seven percent of patients underwent anorectal manometry more than once. A paired student t-test of individual results again failed to identify a significant difference between the maximum resting anal pressure at one assessment compared to another.

Rectal sensation and capacitance was assessed with balloon manometry. A balloon was attached to the end of the manometry catheter. The balloon was inflated and the patient reported first rectal sensation, the first urge to defecate and the maximum tolerated urge to defecate. The balloon volumes at each of these points was recorded. This investigation was not performed in those patients investigated in Chapter 1. All investigations were performed by one assessor [MK].

Pudendal terminal nerve motor latency was assessed with a St Mark’s electrode. Rectal electro-sensitivity was assessed with a urethral ring electrode. To eliminate inter-observer variability, both of these investigations were performed by one assessor only [MK].

**Endoanal Ultrasound**

Anal sphincter integrity is assessed with endoanal ultrasound. A 7.5 Hz linear probe (Aloka) was used in the studies that comprise this thesis.
Pathophysiology

Acute and Chronic Anal Fissures

An anal fissure is a linear ulcer in the anal canal which most commonly presents with the symptoms of severe defaecatory anal pain and bright rectal bleeding. Although 30% of anal fissures have been shown to occur in the presence of a low to normal anal sphincter pressure (Minguez 2002), the hypothesis has been that internal anal sphincter hypertonicity results in anal canal ischaemic injury. In the posterior midline, anal canal arterial perfusion is dependent upon small branches of the inferior rectal artery which pass through the IAS (Shouten 1994). Sphincter hypertonicity is thought therefore to reduce mucosal blood flow. Whether sphincter hypertonicity is the primary pathology or whether it is secondary to local defaecatory trauma continues to be debated (Kuypers 1983). Irrespective of the primary event, mucosal ischaemia is hypothesized to result in non-healing of the ulcer and progression to a chronic anal fissure. Studies have shown evidence of abnormal muscular activity, specifically increases in slow wave and ultra-slow wave activity in patients with sphincter hypertonicity (Gibbons 1986). This, combined with a reduction in resting pressure following internal sphincterotomy (McNamara 1990), a highly successful treatment for anal fissure (Littlejohn 1997), has prompted support for theory that sphincter hypertonicity is the primary pathology.

The focus of treatment has therefore been chemical relaxation of the internal anal sphincter (Lund 1996). Nitric Oxide has been shown to be a significant local neuro-transmitter in the IAS and consequently several treatments have attempted to augment its production. All treatments so far have had a limited success (Shub 1978, Dorfman 1999). One reason for the failure is likely to be the lack of understanding of the neuromodulation pathways and mediators in the internal anal sphincter. Chapter one re-examines the accepted aetiology of anal fissure in light of manometric evidence that fissure healing occurs irrespective of pressure reduction. Glyceryl trinitrate, a stimulator of nitric oxide production is shown not to significantly reduce resting anal pressure in the
20 minutes following application as previously suggested. Botulinum toxin, another treatment thought to augment fissure healing via pressure reduction is shown to heal fissures dependent upon the pre-treatment resting anal pressure but not pressure reduction. The effect on tissue nitric oxide levels of a new method of inducing nitric oxide, inter-sphincteric injection of an adenovirus labelled with inducible nitric oxide is investigated and shown to be ineffective. Finally, a third manometric wave form, the fast wave in the hypertonic internal anal sphincter is validated.

**Faecal Incontinence**

The true prevalence of faecal incontinence is much higher than previously recognised. Early studies of patients obtained from general practitioner groups reported faecal incontinence rates from 1.4-3.1% (Thomas 1984, Campbell 1985). Studies which have examined the prevalence in random population samples have found much higher rates of 12-15% (Roberts 1999, Lam 1999). The two population-based studies carried out in Australia have both found faecal incontinence in over 10% of women (Lam 1999, Kalantar 2002).

Faecal continence is maintained by an interplay of complex activities relying upon sufficient rectal reservoir, normal colonic and rectal transit, adequate discriminatory anorectal sensation, coordinated inhibition of the puborectalis muscle during defaecation, sphincteric integrity and an appropriate stool consistency. Failure in any component can lead to incontinence. Faecal incontinence reaches its peak incidence in the 5th to the 6th decade when there has been a cumulative effect of vaginal delivery, hormonal changes and progressive age-related neuropathy (Vaizey 1997). An ultrasonographically detected sphincter defect may then become a significant contributing factor to the process leading to incontinence (Jameson 1994).

Damage to the internal anal sphincter, intrinsic or iatrogenic, may lower resting pressures resulting in passive faecal incontinence. Damage is most frequently associated with obstetric injury (Sultan 1993). Obstetric perineal trauma may result from at least two mechanisms: neural damage or anatomical disruption of
the sphincter muscles. In the first mechanism, the pudendal nerves may be stretched or trapped as a result of pressure from the baby’s head against the bony pelvis. The resulting nerve damage may be measured objectively using trans-rectal studies of pudendal nerve motor latency (Swash 1985) or by studying anal mucosal electrosensitivity as a measure of the sensory component the pudendal nerves (Sigel 1951). This pudendal neuropathy causes low anal squeeze pressures and decreased anal canal sensation (Kiff 1984, Rogers 1988). This leads to urge faecal incontinence, which may only become manifest some years after childbirth, even in old age.

Pudendal nerve latencies have been shown to be prolonged in 16% of women immediately following vaginal delivery (Sultan 1994). Factors predisposing to nerve damage are prolonged second stage of labour, high birth weight infants, and the use of forceps for delivery (Snooks 1986, Donnelly 1998). Nerve damage is not observed in women undergoing elective caesarean section (Sultan 1993, Donnelly 1998, Reiger 1998). In women who commenced labour and then proceeded to an emergency caesarean section, pudendal nerve latencies were also increased and there was a significant lowering of the perineal plane on straining (indicating pelvic muscle weakness) (Sultan 1993, Sultan 1994). It appears therefore that the nerve damage begins prior to the actual delivery. Prevention of this nerve damage has not been investigated, but if the mother’s choice is vaginal delivery, this is one factor in the causation of faecal incontinence which is possibly not avoidable.

One study comparing continence in patients 30 years following Caesarian Section or vaginal delivery found that there was no statistical difference in frequent flatus incontinence. However, a statistically greater number of women who delivered vaginally (58.6%) reported that their flatus incontinence negatively impacted on their quality of life. Only 15.2% of women delivered by Caesarean Section reported this to be a problem. Furthermore, there was a statistically significant increase in faecal incontinence in those patients who underwent an episiotomy at vaginal delivery (18%). There was no reported faecal incontinence in those women who had undergone a Caesarean Section (Nygaard 1997).
Anatomical trauma occurs with disruption of either the internal or external anal sphincters, resulting in passive or urge incontinence respectively. Several recent studies have shown that 0.5-6% of women delivering vaginally will have a clinically apparent 3<sup>rd</sup> or 4<sup>th</sup> degree tear (Sultan 1993, Jander 2001, Zetterstrom 1999<sup>2</sup>, Hander 2001, Abramowitz 2000). Of even more concern, however, is the rate of tear detected on ultrasound examination. Over the past decade several studies have applied the technique of intra-anal ultrasound to assess anal sphincter injury during childbirth. These studies report that 35-44% of post-partum women will have sphincter disruption on ultrasound (Abramowitz 2000, Faltin 2001, Benifla 2000, Zetterstrom 1999<sup>1</sup>) confirming Sultan's original observation that only 3% of sphincter injuries are clinically detectable (Sultan 1993). This is particularly the case with internal sphincter injuries where the perineum is often intact.

In NSW in 2000, 4.3% of women, 2495 in total, were reported to have clinically detected 3<sup>rd</sup> or 4<sup>th</sup> degree tears (New South Wales Mothers and Babies Report). If one accepts the rates of sphincter damage reported in the literature, this equates to 25,527 women in NSW who will have had a sphincter injury resulting from vaginal delivery in that year.

How many women having sphincter disruption will progress to develop faecal incontinence continues to be debated. 13-24% of post-partum women will report new symptoms of incontinence (Abramowitz 2000, Zetterstrom 1999). There are difficulties correlating sphincter damage on ultrasound with symptoms of incontinence; while 50-90% of women with post-partum incontinence will have a defect detected on ultrasound (Sultan 1993, Burnett 1991), only 37-45% of women with an ultrasound detected defect will report symptoms of incontinence (Reiger 1998, Farnell 1996). Nonetheless, two prospective trials which have examined this issue have all documented a significant correlation between sphincter defects and incontinence symptoms, as well as between the degree of the defect and the severity of the symptoms (Sultan 1993, Faltin 2001).
The absence of reported symptoms in some women with sphincter defects may firstly be explained by the documented reluctance of patients to report symptoms of faecal incontinence. In the general population less than three percent of post-partum women with incontinence will actively seek medical advice (Wood 1998). When they do seek advice, less than five percent of doctors will record the symptoms in the medical record (Soffer 2000). Secondly, those patients who have sphincter defects detected on ultrasound may have sufficient residual function to initially maintain continence but may develop incontinence at a later time. It is this group which needs long-term follow-up.

However, faecal incontinence may also be secondary to perineal surgery or trauma. Non-structural dysfunction, either primary myopathy or age-related degeneration has also been identified as a contributing factor (Vaizey 1997). In the age-related degeneration, microscopy has identified disruption of the normal architecture with smooth muscle cell atrophy and necrosis and extensive collagen deposition (Swash 1988, Speakman 1995). Surface EMG has shown the absence of electrical activity or a reduction in slow-wave activity (Lubowski 1988). Pharmacological abnormalities have also been identified. IAS contractile activity is reduced in response to stimulation with noradrenaline (Speakman 1990). Physiological studies have also identified an increased number of spontaneous relaxations of the IAS and that those relaxations occur at lower rectal volumes (Read 1983). Chapter 3.1 assesses the relative impact of the above predisposing risk factors for faecal incontinence.

**The cost of treatment for faecal Incontinence**

Those costs that are readily accountable include physician consultations, baseline investigations such as flexible sigmoidoscopy, anorectal physiology, ultrasound and defaecography and a short course of biofeedback. These alone total A$1,030.00 per patient based on 2002 Medicare rates. Further patient costs include incontinence pads estimated at A$233.65 per patient, per annum, travel costs, pharmaceuticals, increased laundry costs and time lost from work. A Swedish study estimated that the lifetime cost of these expenses totalled A$17,770(1998) per patient (Adang 1998).
The surgical costs of incontinence treatment vary considerably. An American study estimated that the costs of surgery alone totalled A$9,055.00 (1996) (Mellegren 1999). However, this did not include procedures such as dynamic graciloplasty and artificial bowel sphincter. The former has been estimated to have a lifetime cost of over A$46,000.00 (Adang 1998). Moreover, surgical intervention is successful in less than 50% (Malouf 2001). For those patients for whom the final outcome is stoma formation, their lifetime costs further increase to A$103,800 (Adang 1998).

These costs do not include the psychosocial costs of embarrassment, stigmatization, lost employment, poor maternal bonding, marital stress, the resultant depression and reduced quality of life and the impact on other family members. Nor do they include the cost of premature nursing home placement or the increased demand on community nursing and medical services.

Extrapolating from an Australian study on urinary incontinence costs, at a prevalence estimate of up to 36%, the cost of faecal incontinence secondary to obstetric injury in the community-dwelling woman, at a prevalence estimate of 11% is A$103,423,379.00 per annum (Doran 2001). Given that all of the studies report concern that their total costs are under-estimated with several costs such as the cost of repairing the primary obstetric injury, these figures represent a phenomenal burden on the Australian community.

Consequently, new treatment modalities for faecal incontinence are constantly being explored and old treatments reappraised. Endo-anal ultrasound performed six weeks after a post-partum anal sphincter repair has found that 55-85% of women will have a persistent sphincter defect (Sultan 1994, Nielsen 1992). Delayed primary surgical repair of the internal anal sphincter is successful in less than 60% of patients at five years (Malouf 2000). Re-repair is currently undertaken but the outcome following this procedure has not been previously published. Chapter 3.3 investigates the outcome of sphincter re-repair five years following re-operation. Dynamic Graciloplasty, another surgical treatment transposes the gracilis muscle to reconstruct the anal sphincter.
complex (Baeten 1991, Williams 1991). Recent publications suggest that the longer-term results following this procedure are poor (Baeten 2000, Wexner 2002). An indepth assessment of the long-term efficacy of dynamic graciloplasty neosphincter reconstruction when performed in this Coloproctology Unit is provided in Chapter 3.2. Magnetic stimulation of the pelvic floor augments internal and external sphincter activity (Morren 2001, Shaffik 2000). Magnetic stimulation via a Chair apparatus, a completely new treatment modality is assessed in Chapter 3.4. Sphincter preservation, using minimal surgical intervention in anal Crohn’s disease, is explored in Chapter 3.5.

Rectocele and Global Pelvic Floor Dysfunction

The pelvic floor is a single complex anatomical structure whose function is integrally related to bladder, bowel and sexual organ function. Consequently the effects of pelvic floor weakness frequently manifest as multi-organ dysfunction. By 50 years of age 30-50% of women will have more than one symptom of pelvic floor dysfunction (Steiner 1998, Meshia 2002). Overall, each woman has an 11% life-time incidence of requiring surgery for one symptom of pelvic floor weakness (Olsen 1997). Up to 24% will have concomitant symptoms of bladder, bowel and sexual organ dysfunction (Meshia 2002).

A rectocele is a posterior vaginal wall prolapse which is present to some degree in over 40 percent of women. It has been hypothesised that high IAS pressure may result in an increase in the rectal pressures. This pressure augmentation may over time weaken the perineal fascia and thus allow the development of a rectocele. Chronic constipation has been implicated as one cause for insufficient IAS relaxation and high rectal pressures (Kamm 1989). However controversy continues over the pathophysiology, the clinical significance of defaecation disorders in the presence of a rectocele and the best treatment (Khan 1998, Boccasanta 2001).

Patients with a rectocele may present with obstructed defaecation with or without faecal incontinence. Recent MRI images have suggested, that although
internal or external sphincter defects may contribute to incontinence symptoms in patients with a rectocoele, there is also often global pelvic floor weakness involving ballooning of the puborectalis muscle, marked depression of the levator plate posteriorly and of the levator muscles bilaterally (Steiner 1998). A significant number of patients will also have altered rectal sensation as a result of pudendal neuropathy (Snooks 1985, Kiff 1984). Patients are therefore much more likely to present with multiple symptoms of global pelvic floor dysfunction including genital prolapse and urinary dysfunction (Meschia 2002, McHugh 1987). Unfortunately until recent times the rectocoele was treated by the coloproctologist, the urinary dysfunction by the urologist and the vaginal prolapse by the gynaecologist. This compartmentalisation of the pelvic floor has limited our understanding of the global function of this organ. Furthermore, surgical correction of one compartment has often resulted in deterioration of the function of the adjacent compartment. One example is the high rate of dyspareunia following rectocoele repair (Van Damm 2000).

We are only just beginning to appreciate the factors which contribute to pelvic floor dysfunction. Vaginal delivery again appears to be a significant contributory factor. Up to one third of multiparous women have urinary stress incontinence (Kunskar 2000, Millard 1998). The pathophysiology is very similar to that found in patients with faecal incontinence due to pudendal neuropathy. The striated component of the urinary sphincter is supplied by the perineal branch of the pudendal nerves (Pemberton 2001). Pudendal neuropathy results in perineal (and urethral) descent and urethral sphincter weakness with consequent urinary stress incontinence (Smith 1989).

Hysterectomy, performed in 40% of the women studied in this thesis, is also a significant co-factor in the development of both urinary incontinence and obstructed defaecation (Brown 2000). This is thought again to be due to pudendal nerve injury at the time of surgery. Previous pelvic surgery, in an attempt to correct what is often thought to be an isolated pelvic abnormality, also negatively impacts on pelvic function with 30% of women reporting denovo symptoms of urinary or faecal dysfunction following reconstructive surgery for one or more symptoms of pelvic dysfunction (Abdel-Fattah 2004).
There is no consensus as to the best treatment for these conditions and surgery is complex. Currently rectoceles are repaired via a transanal, transvaginal, transperineal, abdominal or laparoscopic technique. However as our understanding of the pelvic floor as a single function unit has increased there has been increasing interest in fascial specific repairs both for rectocele repair and global pelvic floor dysfunction (Singh 2003, Porter 1999). The laparoscopic approach aims to repair the fascial defects observed from above the pelvic floor (Steiner 1998). The senior author in Chapter 4 developed and adopted the laparoscopic approach to the pelvic floor for correction of posterior compartment dysfunction in accordance with Delancey’s anatomical description of the three levels of vaginal support and rectocele formation. There is currently little data available on the outcome of the laparoscopic repair of clinically significant rectoceles, nor a comparison with the transanal approach (Paraiso 1999, Lyons 1997). There is also no published data on the symptomatic outcome across the pelvic floor compartments in these patients. Chapter 4 addresses these issues.

Summary

Several of the concepts defining anorectal function remain controversial. These concepts however form the basis of the proposed pathophysiology of several disease processes. The following chapters question several aspects of these propositions in a selection of inter-related ano-rectal conditions. Each chapter represents a completed manuscript which has been submitted for publication. Where the review process has been completed and the manuscript accepted for publication, this is stated at the beginning of each chapter.
2.1 Manometric effect of topical Glyceryl Trinitrate and its impact on chronic anal fissure healing

2.2 Prospective manometric assessment of Botulinum Toxin and its correlation with healing of chronic anal fissure
Abstract published in Colorectal Dis 2004; 6(suppl 1): 30
Paper awarded Mark Killingback Prize for Colorectal Research at the Australian and New Zealand College of Surgeons Annual Scientific Conference, Melbourne, May 2004.]

2.3 Adenoviral iNOS gene transfer in the rat internal anal sphincter: impact on tissue nitrate levels

2.4 The High Frequency Wave Form (Fast Wave) in the hypertonic internal anal sphincter: Validation of a new observation.
[Published as Thornton MJ, Kennedy ML, King DW, Lubowski DZ. Colorectal Dis 2004; 6(suppl 1): 69 ]
2.1. Manometric effect of topical Glyceryl Trinitrate and its impact on chronic anal fissure healing

Abstract

Introduction: The duration of physiological action of topical glyceryl trinitrate in the management of anal fissure has been the source of some controversy. We aim to assess the manometric effect of glyceryl trinitrate on internal sphincter resting tone with continuous monitoring.

Methods: Twenty-seven patients with a chronic anal fissure were assessed with fissure, pain, bleeding and continence scores. Twenty-two were randomized to application of one centimetre of topical 0.2 percent Glyceryl Trinitrate paste, applied to the lower anal canal. Five patients were randomized to application of one centimetre of water soluble lubricating jelly to the lower anal canal. Continuous stationary six radial channel water perfusion anorectal manometry was performed for five minutes prior to treatment and then for a further 30 minutes. The 22 Glyceryl Trinitrate patients were then advised to apply topical 0.2 percent glyceryl trinitrate, three times daily, for 8 weeks. Twenty-four hours after completing treatment all baseline assessments were repeated. The lubricant jelly cohort were not reassessed.

Results: During the initial manometric assessment, twenty-one glyceryl trinitrate patients (95 percent) had 20 percent or more reduction in mean and maximum resting anal pressure following treatment. However, there was no statistical difference at 20 minutes compared to 0 minutes (p>0.1). Following eight week’s treatment 16 patients (73 percent) reported symptom resolution and 15 (67 percent) were found to be healed on examination. Clinical healing and resolution of symptoms positively correlated with a higher pre-treatment maximum resting anal pressure in the mid anal canal (p<0.0001), a lower fissure score (p<0.0001) and a greater percentage reduction of the maximum resting pressure following application of Glyceryl Trinitrate (p<0.001). The mean and maximum RAP at week 8 was not significantly different from the baseline values (p>0.05).
During continuous manometry the resting anal pressure did not significantly change in the patients treated with lubricating jelly.

**Conclusion:** A favourable outcome with Glyceryl Trinitrate treatment is more likely in those patients with a lower fissure score, a higher mid-anal canal resting anal pressure and a greater resting pressure reduction following glycercyl trinitrate application. However, given that the physiological response has resolved in less than 20 minutes the dosing regime should be reassessed.
Introduction:

Chronic anal fissure (CAF) is believed to result from the combination of internal anal sphincter hyper-tonicity, relative ischaemia and anal canal trauma (Hancock 1977, Gibbons 1986, Shouten 1994, Lund 1999). Consequently resting anal pressure (RAP) reduction has been the focus of therapy for CAF (Maddoff 2003, Jonas 2001). Glyceryl Trinitrate (GTN) has been demonstrated to reduce internal anal sphincter resting pressure within twenty minutes of application (Loder 1994, Altomare 2000). Despite the acute manometric effect, clinical response to GTN varies widely. While several studies report healing rates no greater than placebo (Altomare 2000, Pitt 1999), other studies report CAF healing rates of up to 80 percent (Oettle 1997, Bacher 1997). The discrepancy may be partly due to the pharmokinetics of GTN which continue to be debated. The manometric effect is reported to last between twenty minutes (Lund 1997) and eight hours (Loder 1994). Given that current prescribing guidelines recommend application three times daily, the manometric and clinical effectiveness of GTN requires further investigation.

This study reports the acute manometric effect of GTN on internal anal sphincter resting pressure and correlates this effect with the clinical response following 8 weeks of GTN treatment.

Methods:

Twenty-seven patients with CAF gave written consent. Linear analogue pain and bleeding scores, a modified St Mark’s continence score (Vaizey 1997, appendix 1) and fissure grading were completed prior to treatment. The fissure grade was assessed by two independent observers [DK,MT] with the patient in the left lateral position prior to any manipulation of the anal canal. The scoring system accounts for the degree of internal anal sphincter exposure on a scale of zero to four (0=healed; 1=fissure with IAS muscle exposed; 2=deeper fissure with IAS deeply exposed; 3=deep undermined fissure; 4=deep undermined fissure plus abscess or fistula). The continence scoring system grades patients from zero to 24, with zero being perfect continence and 24 being daily
incontinence to solid stool. All patients had pre-treatment stationary, six radial channel, water perfusion anorectal manometry with computer acquisition and analysis of data (Neomedix, Sydney, Australia). The cranial distance between the six manometry channels was 0.75cm, such that the pressure was measured from 0.75cm to 3.75cm from the anal verge. The sixth channel measured rectal pressure. The manometry catheter was then taped to the patient's buttock to minimise catheter movement. During continuous manometry, patients were in the left lateral position and were asked to relax and to avoid movement, including conversation.

The patients were randomized via a computer data system. The clinician performing the anorectal manometry [MK] was blinded as to the treatment group. Twenty-two patients had 1cm of 0.2 percent GTN paste (0.5g) [Cellegy, Edgecliff, New South Wales, Australia] digitally applied to the lower anal canal and anoderm. Five patients had 1cm of water soluble lubricating jelly similarly applied. Resting anal pressure was then recorded continuously for 30 minutes. The volume of water infused during manometry was recorded for each patient.

Of the five patients treated with lubricating jelly, 2 were male, median age was 46 (range 27-70), all fissures were in the posterior midline, two were grade 2 and one each were grade 1 and 3. These patients were recruited to control for the potential manometric effect of the 30 minutes of continuous water infusion into the rectum. These patients were discharged from the trial at the completion of the initial manometric assessment.

The twenty-two patients treated with GTN, 14 male, median age 42 (24-69) were recruited with intention to treat. All fissures were in the posterior midline. Six were grade 1 fissures (27 percent), 10 were grade 2 (45 percent) and six were grade 3 (27 percent). Patients were advised to re-apply GTN three times daily for 8 weeks. They were also advised to eat a high fibre diet and were prescribed fibre supplements if constipation was reported at presentation. Patients were also encouraged to complete a daily treatment diary. On the day following completion of eight weeks of treatment all baseline parameters were
repeated. No patient had applied GTN on the day of final assessment. Patients were also questioned about treatment side-effects.

Maximum resting pressure in each physiology channel was measured at two minute intervals from the continuous trace. The six values at each time interval provided a mean and absolute maximum resting anal pressure for statistical comparison. To detect a 20 percent reduction in RAP at a significance of 0.05, 20 patients were required for treatment.

All protocols were approved by the South Eastern Area Health Service Ethics Committee.

**Statistical Analysis**

All parameters assessed before and during GTN treatment were compared with the paired student t-test. Manometric parameters in the lubricating jelly group were assessed with Wilcoxin Log Rank Sum test. A p value <0.05 was considered significant (two-tailed). Group comparisons were performed using a Mann-Whitney U test. Univariate and multivariate analysis was performed with linear stepwise regression utilising SPSS statistical software [SPSS Ptd, version 11, Chicago, Illinois, USA].

**Results** N=27 (all patients)

The mean and max RAPs were 79.5±51cmH20 and 125.6±55cmH20 respectively. The baseline MRAP did not differ between the treatment groups (76.3±52cmH20 GTN, 75.73±47.7 cmH20 lubricating jelly p=0.918). The high pressure zone was in the mid to upper anal canal 2.25 to 3.0cm from the anal verge [fig 1].
The bell-shaped pressure curve was particularly obvious in those patients with a higher RAP. The mean volume of fluid infused through the system was 17ml (14-19ml).

The baseline fissure grade, pain, bleeding and continence scores did not significantly differ between the treatment groups (p= 0.79).

N=5 (lubricant jelly cohort)
During continuous manometry there was no significant change in the mean or maximum RAP (p=0.568).

N=22 (GTN cohort)
Following the first GTN application twenty-one patients (95 percent) had 20 percent or more reduction in the mean and maximum resting anal pressures (mean 39 percent, range 25-71 percent). The reduction in mean RAP was significant two minutes after GTN application and remained significantly lower until 20 minutes of recording. The reduction in maximum RAP was statistically significant at two, ten, sixteen and eighteen minutes but not thereafter [Table1].
Table 1: Mean and Maximum resting anal pressure in both treatment groups over time. p= statistical difference of the value given compared to the baseline, time 0 mins, s= <0.05, ns=>0.05

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</table>

Although a reduction in maximum RAP was seen across channels two to six (ie the length of the anal canal) the only statistically significant reduction was seen in channel 4, 2.25cm from the anal verge [Fig 2]. The rectal pressure did increase during the continuous manometry but not significantly.

All patients were available for follow-up. Treatment diary assessment showed an 87 percent compliance with three times daily GTN application. After 8 weeks of GTN 16 patients (73 percent) reported complete symptom resolution and 14 (64 percent) of these had a healed fissure on examination. There was no deterioration in anal continence. Five patients (23 percent) reported treatment related head-aches controlled with simple analgesia such as paracetamol. At follow-up there was no change in the mean RAP compared to baseline assessment (76.3±52cmH₂O, t₀ vs 77.9±49.9 cmH₂O, t₂₄).

Clinical healing and resolution of symptoms positively correlated with a higher pre-treatment maximum RAP in the mid anal canal (p<0.0001), a lower fissure score (p<0.0001) and a greater percentage reduction of the maximum RAP following application of GTN (p<0.001). A higher baseline RAP and greater percentage RAP reduction after GTN application were significant on multivariant analysis.
Figure 2: Maximum resting anal pressure in all manometry catheters from baseline until 20 minutes after GTN application. Change in maximum resting anal pressure is only significant in channel 4, 3.0cm from the anal verge.

Discussion:

Although GTN results in fissure healing in 27-80 percent (Pitt 1999, Oettle 1997), two large randomised controlled trials report GTN to be no more effective than placebo, irrespective of dose or treatment interval (Altomare 2000, Bailey 2002). This is despite an earlier finding that GTN has a dose dependent effect on MRAP (Hechtman 1996). The minimum dosing interval assessed however was eight hourly. The one study reporting an eight hour RAP reduction after GTN only included 2 patients, the dose was not quantified and the manometry was recorded at selected intervals only (Loder 1994). Subsequent studies report a much shorter duration of RAP reduction. Lund et al assessed continuous anorectal manometry, 20 minutes before and forty minutes after GTN. They report a significant decrease in maximum RAP at 20
minutes but do not comment on the RAP after this time (Lund 1997). The same research centre then reported a RAP reduction for less than 90 minutes (Jonas 2001²). Guillemont reported a RAP reduction for less than 48 minutes despite using ten times the standard dose of GTN (Guillemont 1993). Similarly Cundall et al report less than 80 minutes duration using twice the standard dose (Cundall 2001). In 2001 Jonas et al suggested that the dosing intervals of GTN required re-assessment (Jonas 2001²). Jonas also suggested several co-factors which may have impacted on the earlier results which we have addressed below.

We specifically chose stationary anorectal manometry. The pull-through technique used in some earlier studies (Brisinda 1999) has been shown to stimulate the internal anal sphincter, artificially raising RAP (Rao 1999, Sun 1989). Furthermore, our experience is that patient distraction with catheter movement or involvement in conversation can impact on the RAP. While maintenance of a stationary environment may be criticised as not reflecting normal activity, the purpose of the study was to assess the duration of the pharmacological effect on resting anal pressure.

The placebo, lubricating jelly cohort, were included in attempt to control for another co-factor. During 30 minutes of continuous anorectal manometry an average of 17 ml of fluid is infused through the system. While some of this fluid will drain out of the anal canal we were concerned that in the hypertonic anal sphincter more of this fluid would be retained in the rectum. The increased rectal volume could potentially stimulate the anorectal inhibitory reflex lowering the anal canal pressure irrespective of treatment. The results of the placebo group suggest the infusion volume is not a confounder.

The placebo cohort were not followed longer term because several randomised controlled trials have shown that fissure healing rates following treatment with placebo or GTN are no different (Altomare 2000, Pitt 1999, Kennedy 1999). Our results showing a positive correlation between healing following GTN treatment and a lower fissure score may suggest one reason for this. Although there are no studies confirming that lower grade fissures are more likely to heal,
histologically they demonstrate less fibrosis and disturbance of the internal anal sphincter fibres than higher grade fissures (Gibbons 1986). It may be that avoidance of further mucosal trauma with the use of laxatives would allow low grade fissures to heal irrespective of other treatment modalities.

Another criticism may be the magnitude of RAP reduction assessed to be statistically significant. We did not find the RAP reduction to be significantly different at 20 minutes despite the absolute values continuing to be 8 to 10cmH\textsubscript{2}O lower. While statistical significance may not reflect clinical significance this study was powered to detect the minimal RAP reduction previously shown to augment internal anal sphincter perfusion (Bailey 2002). If the hypothesis of ischaemia secondary to anal sphincter hypertonicity is correct, a 20 percent RAP reduction should be a valid statistical end-point.

Although not a primary aim of the study, the internal anal sphincter pressure wave distribution found in this study has previously been described by Keck (Keck 1995). They also noted that CAF patients have a bell shaped pressure wave with the maximum RAP recorded in the mid-anal canal. Conversely, normal patients were found to have a bell curve skewed to the right with the maximum RAP recorded in the distal anal canal. This difference in pressure wave distribution, in particular the site of the peak of the curve, may impact on the clinical efficacy of GTN. We found that those patients with a higher RAP in the mid-anal canal were statistically more likely to demonstrate a greater percentage RAP reduction following GTN application and were more likely to heal with GTN treatment.

Our side effect profile is lower than previously reported both for faecal incontinence (Carapetti 1999) and treatment limiting headaches (Pitt 1999, Lund 1997, Zuberi 2000). Treatment diary assessment and clinical healing suggests this does not reflect treatment non-compliance. The methods of assessment were standardised and had been previously employed by the authors (Kennedy 1999, Thornton 2004). The reason for the difference is difficult to explain.
We are not the first to report no RAP reduction after completion of GTN nor is the result surprising given GTN's duration of action (Kennedy 1999). Despite this we report 64 percent CAF healing with three 20 minute intervals of RAP reduction per day for 8 weeks. We also report the effect to be greater in those with a lower fissure grade, higher RAP and greater percentage reduction. Although a dose-dependent response is recorded (Cundall 2001), increasing the dose by even 10 times does not increase the duration of effect to greater than 80 minutes (Bailey 2002, Guillemot 1993). Furthermore, decreasing the dosage interval from 12 to eight hourly does not increase healing rates (Cundall 2001). Given the short duration of action of GTN it remains to be assessed whether application of GTN at much shorter intervals will result in increased healing rates, particularly in those patients identified in this study to be more receptive to GTN treatment. However it is likely that frequent GTN application will be inhibited both by the reported side effect profile and tacchyphylaxis. The healing rates following treatment with GTN are therefore unlikely to far exceed that of a placebo.

Conclusion:

GTN has a limited duration of action on internal anal sphincter resting pressure. Application three times daily will result in healing in 63 percent of patients, little more than placebo. However, healing positively correlates with a lower baseline fissure score, a higher mid-anal canal RAP and a greater percentage RAP reduction.
2.2. Prospective manometric assessment of Botulinum Toxin and its correlation with healing of chronic anal fissure

Abstract

Introduction: The efficacy and pharmacokinetics of botulinum toxin (BT) treatment for chronic anal fissure (CAF) continues to be debated. Addressing both issues we prospectively assessed the manometric impact of BT on internal anal sphincter (IAS) pressure, correlating this impact with CAF healing.

Methods: Sixty patients with CAF were assessed. Fifty-seven patients had a total of 20 units of BT injected into the intersphincteric groove at 4 and 8 o'clock. Patients were prospectively assessed with a linear analogue pain score, bleeding score, clinical fissure score, modified St Mark's continence score and anorectal manometry. Each parameter was reassessed two weeks following treatment and again at three months.

Results: Fifty-six patients (30 female), median age 43 (range 17-80) were followed for a median of five months with fissure healing assessed 12 weeks after treatment. (range 3-15). Physical healing and symptom control were related to the baseline maximum resting anal pressure (MRAP) and baseline fissure score (p=0.003, p=0.009 respectively). Although MRAP fell by 17 percent (range 0-71 percent), MRAP reduction did not correlate with clinical outcome (p>0.2). Seventeen patients reported a mean 17 percent increase in continence score. There was no correlation between deterioration in continence and baseline or subsequent reduction in MRAP.

Conclusion: Patients with grade 1, lower pressure fissures are more likely to heal following treatment with 20 units of BT. Healing does not appear to be dependent on a reduction in MRAP.
Introduction

Up to 70% of patients with chronic anal fissure (CAF) will have a hypertonic internal anal sphincter (IAS) (Hancock 1977). It is unclear whether this hypertonicity precedes or results in anal fissure (Gibbons 1986, Lin 1989, Nothmann 1974, Chowcat 1986). Nitric Oxide (NO) is the principle nonadrenergic, noncholinergic neurotransmitter in the IAS and its release results in IAS relaxation (O’Kelly 1993, Rattan 1992). It was suggested that Botulinum Toxin (BT) increases local release of nitric oxide (Mariotti 1996). BT was therefore introduced as a therapy for CAF on the premise that it would reduce IAS tone and promote fissure healing (Jost 1994, Gui 1994). However, recent research questions both the nitric oxide and earlier cholinergic neurotransmitter hypotheses, suggesting BT’s mechanism is sympathetic ganglion blockade, even though sympathetic ganglia have not been identified in the internal anal sphincter (Jones 2003, Jones 2004). The identification of anti-endothelial cell antibodies in CAF also raises doubt as to the current explanation of BT’s pharmacokinetics (Maria 1999).

While several authors report a reduction in mean maximum resting anal pressure (MRAP) following BT, it is not possible to ascertain from these reports whether MRAP reduction correlates with clinical outcome for the individual patient (Minguez 1999, Brisinda 2002, Brisinda 2004). Maria et al reports a mean MRAP reduction following BT but for at least 4 out of 15 patients fissure healing occurred without a MRAP reduction (Maria 1998). The reported effect of BT on MRAP and CAF healing are controversial. Brisinda et al has recently suggested that their results demonstrate a dose dependent reduction in mean MRAP and yet this research group also reported no change in MRAP with higher treatment doses (Brisinda 2004, Maria 1998). Minguez et al reported a dose-dependent effect on MRAP but no significant difference in patient outcome (Jones 2001).

We report the physiological impact of BT on MRAP in CAF patients. In an attempt to address the issues raised above we have correlated the
physiological effect with patient pre-treatment parameters and post-treatment outcomes.

Patients and Methods

All CAF patients presenting between June 2002 and June 2003 were assessed. Chronicity was defined as non-healing of the fissure following a six week course of Glyceryl Trinitrate (GTN) [Cellegy, Edgecliff, New South Wales, Australia], if clinically tolerated (Maria 1998). Patients with a history of recent anal surgery or peri-anal sepsis were excluded. The presence of a fistula originating from a posterior fissure was not an exclusion criteria. Pregnant and breast-feeding patients were excluded.

Prior to treatment patients were assessed with a linear analogue pain score, with zero being no pain and ten being the worse pain ever experienced. The presence of bright red defaecatory bleeding was also assessed. Patients also completed a modified St Mark's continence score which grades continence from perfect (score of 0) to daily incontinence to solid stool and the inability to defer defecation for more than fifteen minutes (score of 24) (Vaizey 1997, appendix 1). The fissure was then graded based on the presence of exposed IAS fibres [legend Table 1]. Informed consent was obtained for injection of 20 units of BT [Allergen, Gordon, New South Wales, Australia] into the intersphincteric groove in the direction of the IAS, at 4 and 8 o'clock, without sedation or local anaesthetic. A total of 0.4ml of solution was injected with a 22G needle. This was performed by one clinician in the anal manometry clinic.

All patients were advised to eat a high fibre diet and were provided with a prescription for fibre supplements if constipation was reported at presentation. The baseline clinical and manometric assessments were repeated two and ten weeks after treatment. All patient symptoms were assessed longer-term via a telephone interview.

Fissure healing was defined as resolution of the fissure on examination 10 weeks after the final BT treatment. Patients had their physical assessment repeated by the referring consultant in the two weeks after trial completion. The referring consultant was blinded as to the grading given at the first assessment.
Those patients who did not heal were assessed for improvement in pain scores and resolution of rectal bleeding.

Anal manometry was performed with a 5 channel, low compliance water perfusion system as previously described (Kennedy 1999). This system records pressures in the anal canal at intervals of 0.75cm from the anal verge. A sixth channel recorded rectal pressures. Resting, squeeze and cough pressures were recorded.

All protocols were approved by South Eastern Area Health Service Ethics Committee.

**Statistical Analysis**

All parameters assessed pre and post-treatment was assessed with ANOVA. A p value <0.05 was considered significant (two-tailed). Subgroup analysis was performed using a Mann-Whitney test. Linear regression analysis was applied to determine the significance of the baseline fissure score, patient age, MRAP and reduction in MRAP as factors in fissure healing and symptom improvement.

**Results**

Sixty patients (33 female), median age 43 (range 17-80) were referred. Three patients chose not to be treated because of the risk of transient faecal incontinence. One patient withdrew following treatment. Fifty-six patients (30 female), median follow-up 5 months (range 3-15 months), are reported. [Figure 1]
Figure 1. Flow diagram of patient outcomes

Recruitment

60 patients

3 chose not to be treated

57 patients treated BT

1 LTF

2 weeks post-BT

12 symptoms not improved re-treated BT

44 symptoms improved

10 weeks after final BT

56 patients

37 healed

19 not healed

5 bleeding and pain score >5

sphincterotomy

2 bleeding and pain score <5

Re-treated with BT

5 no bleeding, pain <5

Laxatives, analgesia

2 retreated BT

6 symptoms recurred

7 no bleeding and no pain

No treatment

60 patients

Recruitment

2 weeks post-BT

10 weeks after final BT
Baseline Assessment (N=56) [Table 1]
Fifty-three fissures were in the posterior midline. Three were in the anterior midline. Twenty-eight were grade 2 fissures. Defaecatory bleeding was a presenting symptom in 54 patients.
Forty-five patients reported pain scores greater than five. The pain score positively correlated with a higher fissure score (p<0.003) and was associated with the presence of bleeding at presentation(p<0.01).

Table 1: Patient factors across the outcome groups. (mean± 2 standard deviations; MRAP 2 = mean resting anal pressure 2 weeks after treatment, MRAP final = MRAP 10 weeks after final treatment; p value: ns =>0.05, s =<0.05). Fissure Grade: Grade 0 - healed, Grade 1 - fissure with exposed internal anal sphincter (IAS), Grade 2 - deeper fissure with widely exposed IAS, Grade 3 - deep undermined fissure, Grade 4 - associated peri-anal fistula.

<table>
<thead>
<tr>
<th>Factor</th>
<th>All (n=56)</th>
<th>Fissure healed (n=37)</th>
<th>No (n=19)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>n=56</td>
<td>n=37</td>
<td>n=19</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>45±14</td>
<td>45±15</td>
<td>45±12</td>
<td>0.882</td>
</tr>
<tr>
<td>Gender (f:m)</td>
<td>30:26</td>
<td>21:16</td>
<td>9:10</td>
<td>0.505</td>
</tr>
<tr>
<td>Pain score</td>
<td>7.7±2.3</td>
<td>7.4±2.7</td>
<td>8±2.7</td>
<td>0.324</td>
</tr>
<tr>
<td>Fissure Score</td>
<td></td>
<td></td>
<td></td>
<td>0.019</td>
</tr>
<tr>
<td>Grade 1</td>
<td>27</td>
<td>22 (81%)</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>28</td>
<td>13 (48%)</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Grade 3</td>
<td>1</td>
<td>0 (0%)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Bleeding (Yes)</td>
<td>47</td>
<td>36</td>
<td>18</td>
<td>0.115</td>
</tr>
<tr>
<td>MRAP</td>
<td>147±43</td>
<td>139±41</td>
<td>164±44</td>
<td>0.046</td>
</tr>
<tr>
<td>Cough</td>
<td>95±42</td>
<td>100±43</td>
<td>86±41</td>
<td>0.255</td>
</tr>
<tr>
<td>Squeeze</td>
<td>117±46</td>
<td>117±45</td>
<td>119±51</td>
<td>0.879</td>
</tr>
<tr>
<td>Follow-up</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRAP (2)</td>
<td>143±45</td>
<td>147±40</td>
<td>156±46</td>
<td>0.128</td>
</tr>
<tr>
<td>MRAP (final)</td>
<td>134±45</td>
<td>131±47</td>
<td>140±42</td>
<td>0.485</td>
</tr>
<tr>
<td>%reduction MRAP</td>
<td>17±13</td>
<td>15±9</td>
<td>21±18</td>
<td>0.113</td>
</tr>
<tr>
<td>absolute reduction</td>
<td>27±26</td>
<td>37±39</td>
<td>21±14</td>
<td>0.027</td>
</tr>
</tbody>
</table>

Anal Manometry

The median baseline MRAP was 155 cmH₂O (range 64-268 cmH₂O).
Two weeks following BT there was a 10.27 percent mean reduction in MRAP (range 0-47.2 percent). The MRAP fell a further 3 percent in those patients treated with second BT injection. Ten weeks following the final BT injection manometry, repeated in all patients, demonstrated a MRAP mean percentage reduction of 17.1 percent (range 0-57 percent), reducing the median MRAP to 128 cmH$_2$O (range 41-248 cmH$_2$O). Reduction in sphincter pressure occurred along the length of the internal anal sphincter as evidenced by the reduction in MRAP across all anal manometry channels, from 0.75cm to 3.75cm from the anal verge. [Fig 2] The difference between the baseline and final MRAP was statistically significant (p<0.009).

![Figure 2. Change in MRAP across all manometric channels over the trial period.](image)

The median baseline squeeze pressure decreased from 117 to 104.6 cmH$_2$O and the median baseline cough pressure decreased from 95 to 80.95. Neither reduction was statistically significant (p>0.1, p>0.05 respectively).

**Fissure Healing**
Thirty-seven (66 percent) fissures healed and a further eight had a lower fissure score. The final fissure score given by the two observers differed for one patient. Re-examination by the first observer confirmed the finding of the latter. Of the healed fissures, twenty-two were initially assessed to be grade 1 fissures, being 81 percent of all grade 1 fissures, compared to 46 percent of the grade 2 fissures (p=0.019).

Fissure healing was associated with pain improvement (p<0.001) and bleeding resolution (p<0.002). Of the 19 patients who did not heal, seven were symptom free. Each of these patients had a baseline MRAP less than the group median of 155 cmH₂O. In total ninety-six percent (25/26) of patients with a MRAP below 155 cmH₂O reported symptom resolution. This was statistically greater than the number of patients with a MRAP greater than 155 cmH₂O who reported symptom resolution (19/30, p<0.001)[Fig 3].

![Figure 3. 95% Confidence Intervals for baseline MRAP (cmH₂O) comparing patients with and without symptom resolution 10 weeks following final BT treatment.](image)

Of the twelve patients who did not report symptom improvement five proceeded to sphincterotomy. Each of these patients had a baseline MRAP above 179cmH₂O. Two further patients were re-treated with BT after completion of the trial with good effect and five continued to use simple analgesia and laxatives.
No patient with a healed fissure twelve weeks after treatment reported symptom recurrence at the telephone interview.

The baseline MRAP was significantly lower in those patients who healed (p<0.046) [Fig 4]. Although the percentage reduction in MRAP following treatment did not differ between the healed and non-healed groups (p>0.58), the absolute MRAP reduction was significantly greater in the non-healed group. The mean MRAP reduction in the healed group was 21 cmH\textsubscript{2}O compared to 37 cmH\textsubscript{2}O in the non-healed group (p<0.027). Ten weeks after treatment the resultant mean MRAP for the non-healed group was not significantly different to the mean MRAP of the healed group (p=0.485).

![Figure 4: 95% Confidence intervals for baseline MRAP (cmH\textsubscript{2}O) comparing healed and non-healed fissures 10 weeks following final BT treatment.](image)

On multivariate analysis of fissure healing the baseline MRAP and baseline fissure score were found to be significant (p=0.003, p=0.009 respectively). Furthermore, a fissure score of one was a significant predictor of healing in those with a MRAP less than 155 cmH\textsubscript{2}O (p=0.016).

**Side-effects**
Prior to treatment the median continence score was zero (range 0-2). During follow-up continence scores significantly increased in 17 patients (p<0.025). Although the median score remained zero, the mean increased to 2 and the maximum score increased to 20. Three patients became house-bound with continence scores of 12 or greater. One patient also developed urinary stress incontinence. All continence scores had returned to baseline at the telephone interview and the urinary incontinence had settled. There was no statistical association between the baseline MRAP and the development of faecal incontinence, nor with the severity of the incontinence (p>0.09). Nor was there an association between the final continence score and the reduction in MRAP following treatment (p=0.748). The development of faecal incontinence was not associated with a decrease in cough and squeeze pressures (p>0.1).

Two patients reported urticarial rashes during the 48 hours following the treatment. Neither patient had been previously exposed to BT. There was one peri-anal haematoma formation following the injection.

Discussion

Our healing and symptom resolution rates are similar to earlier trials assessing the role of BT in CAF (Maria 1998, Brisinda 2002, Lindsey 2003). Consistent with these trials we also report a significant reduction in mean MRAP (Minguez 1999, Brisinda 2004, Maria 1998, Lindsey 2003). The smaller reduction in MRAP documented in this study may be the result of many co-factors previously described by Brisinda et al, in particular choosing 20 units of BT as the injection dose. The optimal dose and injection site is not known (Madalinski 2002). Minguez found equivocal healing rates whether 10, 15 or 21 units were injected with no change in the side effect profile (Minguez 1999). Subsequent studies however suggest that a higher dose, such as 30 or 50 units, does effect higher healing rates (Brisinda). Doses over 20 units however have been associated with higher rates of transient faecal incontinence (Brisinda 2002). Twenty units was chosen as a safe and effective dose. Despite the lower dose chosen and the smaller reduction in MRAP, we have noted similar clinical results. Not all studies report a dose dependent effect on MRAP, nor a dose
dependent effect on healing (Brisinda 2004, Maria 1998). No previous trial has documented a correlation between the MRAP reduction following BT and fissure healing. This raises two questions. Firstly whether the absolute MRAP is the pathophysiology which needs to be corrected and secondly, the mechanism of action of BT in CAF.

Several treatments for CAF suggest that a hypertonic IAS may not be integral to fissure pathophysiology. Firstly, the tailored anal sphincterotomy has a reported healing rate of 98 percent (Littlejohn 1997) and yet the proximal anal canal pressures, including the high pressure zone (Mentes 2003, Keck 1995) will not be affected because of the limited nature of the sphincter division (Cerdan 1982, McNamara 1990). Secondly, Kennedy et al documented 70 percent healing rates following topical glyceryl trinitrate without demonstrating a significant reduction in MRAP (Kennedy 1999). Thirdly, Minguez and our study report 30 percent of CAF occurring in the normal to hypotonic IAS (Minguez 1999). Finally, the anal advancement flap with reported healing rates of over 80 percent aims to effect a cure without reducing the MRAP (Nyam 1995). Attempting to reduce MRAP alone in order to heal a CAF would seem, in light of this information, to be ignoring another significant factor.

The effect of BT on rectal bleeding is also difficult to explain if hypertonicity is the pathophysiology of CAF. In this study bleeding resolution did not correlate with MRAP reduction. Consistent with our results Brisinda reported resolution of bleeding irrespective of pain scores or fissure healing following BT (Brisinda 1999). The pharmacological effect of BT on the CAF has not been fully explained.

Pre-existing sphincter hypertonicity may however explain the limited efficacy of BT in these patients. IAS hypertonicity has been shown to be associated with reduced perfusion in the anal canal (Shouten 1994, Klosterhalfen 1982, Lund 1999). Reduction in perfusion would result in lower local tissue absorption of the pharmacological agent. Lysy et al reported increased healing with BT when coupled with GTN (Lysy 2001). It was hypothesized in this study that GTN increased the anodermal blood flow thus increasing the efficacy of the BT.
Higher doses of BT in the hypertonic IAS may be required to effect fissure healing in patients with higher anal pressures. Although the number of patients in this trial receiving a second dose was small, 70 percent of these patients healed, despite a further MRAP reduction of only three percent.

One alternative effect of BT may be placebo. Norton et al, reported symptomatic improvement in patients with faecal incontinence irrespective of intervention intensity (Norton 2003). They concluded that the psychological support provided by a consultation was enough to effect a symptomatic improvement. Similarly, the healing rates in this and previous trials may reflect the psychological support provided by follow-up appointments rather than the pharmacological effect of BT. Each appointment provided an opportunity to reinforce the use of fibre supplements, to counsel on avoiding the urge to strain with defecation and to provide reassurance. However, given earlier randomised placebo controlled trials it is more likely that there is a pharmacological mechanism that has yet to be fully elucidated (Maria 1998).

There is little trial evidence supporting the anecdotal observation that fissure chronicity correlates with poorer healing (Cerdan 1982, Lund 1999, Minguez 2002). However a grade 2 fissure is by definition deeper with greater evidence of chronic scarring (Gibbons 1986). It would therefore not be surprising if these fissures were more resistant to healing, as demonstrated in this trial. Although this trial could be criticised for not formally assessing the fissure under anaesthesia, each final assessment, performed by one investigator, was later confirmed by the referring consultant, blinded to the investigator's assessment.

Faecal incontinence is a recognised complication of treating CAF with BT (Minguez 1999, Brisinda 2004). In the current series those patients who became incontinent were not predictable from their baseline MRAP. Similarly, Melange et al investigating the manometric effects of internal sphincterotomy, reported no correlation between MRAP and the development of anal incontinence (Melange 1992). They hypothesized that the incontinence may have been partly due to a reduction in the length of functional sphincter and could therefore be minimized by a minimalist sphincterotomy. However, our
results, like those of Borodic et al, show that BT has a uniform manometric effect along the length of the IAS, resulting in a global weakening rather than a simple reduction in functional length (Borodic 1994). Incontinence following BT may not be avoided simply by dose reduction. Melange was also one of the first studies to recognise that patients do not spontaneously report symptoms of faecal incontinence but rather detailed prospective questioning is required to identify these patients (Melange 1992). The concerning observation in our trial is that with such questioning, we identified young, healthy patients with normal to increased anal sphincter pressures who became incontinent following BT treatment. Conversely, incontinence following internal sphincterotomy is a particular concern in patients with a low MRAP (Nyam 1995, Khubchandanu 1989). Our results suggest that these patients are no more likely to develop incontinence with 20 units of BT than normotonic patients.

Injection into the intersphincteric groove has been hypothesized to result in faecal incontinence as BT diffuses across the external anal sphincter. Brisinda et al first suggested this hypothesis and yet they did not find a significant difference in the squeeze pressure between the group who were more likely to develop incontinence and the group less likely to develop incontinence (Brisinda 2002). Furthermore, their most recent trial demonstrates a 20 percent reduction in squeeze pressures despite injection into the IAS and with no resultant incontinence (Brisinda 2004). Our results add further doubt to the hypothesis as no correlation was demonstrated between the presence of faecal incontinence and a reduction in the squeeze or cough pressures following treatment.

Conclusion

Twenty units of BT is effective management of low grade CAF, particularly in those with a MRAP below 155cmH\textsubscript{2}O. Further investigation is required into the physiological impact of BT on the IAS. We suggest that a reduction in the MRAP may not be the mechanism effecting CAF healing when treated with BT.
2.3. Adenoviral iNOS gene transfer in the rat internal anal sphincter: impact on tissue nitrate levels

Abstract

Introduction: This study was designed to assess anal sphincter nitrate levels following intramuscular adenoviral iNOS gene transfer in the rat internal anal sphincter.

Methods: A randomized double blinded control trial was performed. Eighty Sprague Dawley male rats were randomized to three treatment groups; control, intramuscular iNOS labelled adenovirus and intramuscular placebo-labelled adenovirus. The rats were sacrificed one, seven and twenty-one days following treatment. The rat anal sphincter complex was excised and the tissue nitrate levels analysed.

Results: Tissue nitrate levels did not significantly change in any group following treatment. Tissue nitrate levels following treatment with iNOS or dummy virus were not significantly different.

Conclusion: Transfection with an iNOS labelled adenovirus does not increase nitrate levels in the rat anal sphincter.
Introduction

In experimental cutaneous tissue injury, inducible nitric oxide synthase (iNOS) has been shown to be upregulated within hours of the injury and to remain upregulated for 10-14 days (Yamasaki 1998). The resultant increase in nitric oxide (NO), produced by iNOS, plays many important roles in wound healing, from the inflammatory phase through to scar remodelling [Fig 1] (Calatayud 2001).

Nitric oxide synthase (inhibited by N-nitro-L-Arginine)

\[
\begin{align*}
&\text{L-Arginine} \\
&\downarrow \\
&\text{Oxygen} \\
&\text{NADPH} \\
&\text{Nitric oxide}
\end{align*}
\]

Figure 1: Metabolic pathway for Nitric Oxide

Nitric oxide has cytostatic, chemotactic and vasodilatory effects during early wound repair, regulates proliferation and differentiation of several cell types, modulates collagen deposition and angiogenesis and affects wound contraction (Schwentker 2002, Radomski 1995). Nitric oxide, through one or more of these mechanisms is believed to be critical in the healing of anal fissures (O’Kelly 1993). Therapeutic modalities to augment NO levels include L-arginine supplements, chemical NO donors and gene therapy involving nitric oxide synthase isoforms (Cook 2001). Current research is focusing on NO induction following gene therapy.

Transfection with a gene labeled adenovirus has been shown to increase the transferred gene expression for up to 90 days (Kovedski 1997). Adenoviral iNOS gene therapy has been shown in placebo controlled studies to increase nitrite and nitrate levels, the stable end-products of NO production (Reid 2002). Furthermore mice deficient in iNOS exhibit greater than 30% delay in wound healing which can be corrected with a single application of iNOS via an adenoviral vector (Yamasaki 1998). The aim of this study was to investigate the
effect of intramuscular adenoviral iNOS therapy on the nitrate levels of the rat anal sphincter.

Methods:

Eighty male Sprague Dawley rats were randomised to three treatment groups; no treatment, injection with a placebo labelled viral vector [Ad5-CMVempty] and injection with an iNOS gene labelled adenoviral vector [Ad5-CMViNOS] [Gene Transfer Vector Core, the University of Iowa, Iowa City, Iowa, USA]. These groups were then sub-randomised into pre-determined intervals for tissue analysis.

Ad5CMVntiNOS, a replication deficient adenovirus containing the reporter gene, iNOS, was used for transfection. Ad5CMVempty, the replication deficient adenovirus vector devoid of the exogenous gene, was used to control for any effects caused by the adenovirus transfection alone. Doses of 0.2 millilitres, equivalent to $10^8$ PFU adenoviral vector were prepared by YB, 30 minutes prior to administration, blinding the investigators to the treatment group.

Each rat was treated with the 0.2 millilitres, into the anal sphincter using a 27 gauge needle.

At intervals of one, seven and twenty-one days following treatment the rats were sacrificed with CO$_2$ inhalation. The investigators remained blinded as to which treatment group the rat belonged. Sharp dissection of the rat anal sphincter complex was performed immediately post-mortem. The specimens were frozen and when specimen collection was complete tissue nitrate levels were assessed.

Tissue Nitrate Assessment

The samples are thawed, crushed and transferred into pre-weighed eppendorf tubes. The samples are homogenated. After adding 500µL of water to 50mg of tissue, the samples are sonicated on ice and centrifuged at 15 000 rpm for 15
minutes at 4°C. The supernatants are then transferred to 100mm screw-top glass vials.

For comparison standard samples of 0.2, 1.0, 5, 10, 20 and 100 nmol/50µL [¹⁴N] NaNO₃ are prepared. An internal standard of 200 nmol/ml (µM) [¹⁵N] potassium nitrate is also prepared. 50µL of the internal standard is then added to each of the 50µL standard and samplet tubes.

Each tube is then dried under a Speed Vac Rotary Evaporator (Savant Instruments, Selby Scientific and Medical Clayton, Vic, Australia 3168). One ml toluene and 200µL Trifluoracetic Anhydride (TFAA) is then added to each sample, the tubes capped and heated at 70°C for 60 minutes. After cooling to room temperature, the toluene is washed sequentially with water (1mL), aqueous sodium bicarbonate (1%, 1mL) and water (1mL). The solution is then dried over anhydrous sodium bicarbonate (500mg) and removed to a GC autosampler vial for GC-MS analysis. Activity is detected on a Hewlett Pakard 5973 Mass Selective Detector.

All protocols were approved by the University of New South Wales Animal Care and Ethics Committee.

**Statistical Analysis**

The Statistical Package for Social Sciences [SPSS Ltd, version 11, Chicago, Illinois, USA] was used for data analysis. Non-parametric data was assessed using the Kruksall-Wallis and Mann-Witney tests. A p value <0.05 was considered statistically significant.

**Results**

Twenty rats were randomised to both the control and dummy iNOS treatment groups. Forty rats were randomised to the iNOS labelled adenoviral treatment group. [Table 1]
### Table 1: Number of rats randomised for sacrifice at selected times in the study protocol and NO tissue levels (mean and confidence intervals)

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 7</th>
<th>Day 21</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>CI</td>
<td>Mean</td>
</tr>
<tr>
<td>Control</td>
<td>N=6 111.38</td>
<td>40.47-182.25</td>
<td>N=7 56.5</td>
</tr>
<tr>
<td>Dummy</td>
<td>N=7 79.54</td>
<td>-3.01-162.08</td>
<td>N=7 130.25</td>
</tr>
<tr>
<td>iNOS</td>
<td>N=14 113.45</td>
<td>66.47-160.44</td>
<td>N=14 116.94</td>
</tr>
</tbody>
</table>

The average weight of each rat at the time of randomization was 103.6 grams. One rat in the control group died unexpectedly and was excluded from analysis. One tissue sample from the dummy viral treatment group was lost during processing and was therefore not available for analysis. The results from seventy-eight samples are reported.

The average weight of each rat at the time of sacrifice did not significantly differ between the treatment groups [p=0.67].

Within each treatment group the nitrate level did not significantly change over time [p=0.186 control, p=0.218 dummy iNOS, p=0.404 iNOS ] [Figure 2]

Nitrate levels were significantly higher in the iNOS and dummy iNOS groups at day 21 when compared to the day 7 control group [p=0.013 and p=0.022 respectively]. However, day 21 iNOS nitrate levels were not significantly different when compared with the combined control group nitrate levels [p=0.123]. However, day 21 dummy iNOS levels were significantly greater than the combined control group nitrate levels [p=0.03]. [Figure 3 ]
Figure 2: Mean nitrate and 95% Confidence Intervals for each Study Group

Figure 3: Tissue levels of NO recorded across the treatment groups
Discussion

Previous studies have shown a predictable increase in endogenous NO breakdown products following tissue injury (Calatayud 2001). The levels of nitrite and nitrate are low at three hours following an ischaemic or cutaneous injury, peak at six to nine hours and dissipate at 24 hours (Reid 2002). Following adenoviral stimulation of iNOS the levels of nitrite and nitrate in the inoculated tissue have been shown to double within three hours and remain elevated at 48 hours (Salkowski 1997). High level expression of the transfected gene has been seen at 90 days following treatment (Kovedski 1997, Graham 1995).

Compared to the control group nitrate levels we did not demonstrate a significant increase in nitrate levels following treatment with iNOS labeled adenovirus. There are at least five possible explanations.

The first is a systems error that may have occurred either in vector preparation, tissue storage or tissue processing and analysis. Two treatment sessions and dose preparation less then 30 minutes prior to administration should minimise possible vector errors. The use of two standard, independent nitrate analysis techniques should minimise analysis errors. However the samples were stored until the project was completed and then processed en bulk. It is possible that the nitrate levels were compromised during this interval. Sinc the time of these experiment Daiber et al have documented problems with analysis of nitrination products following freezing (Daiber 2003).

The second explanation is that in the rat anal sphincter iNOS may not be the responsible isoform for the subsequent rise in NO previously documented in anal fissure disease. In the corpus cavernosus endothelial nitric oxide synthase is responsible for the subsequent smooth muscle relaxation (Bloch 1998). Until recently NO was believed to be the substrate in GTN responsible for relaxation of the internal anal sphincter, increased angiogenesis and healing of anal fissures. Recent evidence suggests that NO may not be the principle agent (Kleschyov 2002, Kleschyov 2003).
The third is suggested from previous studies demonstrating a significant difference between the NO production of tissue stimulated with an iNOS and a dummy labelled virus which we were not able to demonstrate. Previous studies have been performed on animals that have been subject to a deliberate tissue insult (Yamasaki 1998, Thornton 1998, Efran 1999, Dai Quan 2003). With the exception of the 27 gauge needle puncture to insert the virus there was no other deliberate or inherent tissue injury. Although studies have demonstrated increased rates of healing following treatment with iNOS gene transfer, the mechanism of the effect has remained unclear.

It is possible that absence of an underlying injury precludes activation of the acute phase reactant cascade and that one of these factors is a necessary constituent for the iNOS induced tissue response (Schwentker 2002, Noiri 1997). Salkowski et al clearly demonstrated that IFN-gamma production was central to both the induction of iNOS mRNA and the accumulation of nitrate/nitrite (Salkowski 1997). The absence of tissue injury may result in lower IFN-gamma levels and therefore iNOS induction and NO production.

The fourth explanation may be that the time intervals selected were beyond the interval when the NO production was increased. Only one study has shown ongoing transfection, although not iNOS expression at 90 days (Kovedski 1997). Other studies have shown a marked reduction in transfected iNOS expression as early as two to ten days (Yamasaki 1998, Reid 2002). It may be that at least for the second and third cohorts treated with the viral vector that expression had dissipated.

The fifth explanation is provided by one of the major disadvantages to adenoviral therapy. In vivo delivery may be hampered by prior immune response to the virus (Croyle 2001). To increase transfection and to decrease host immune systems, adenovirus may be used in conjunction with other agents (Varnavski 2002). Pure adenoviral vectors were used in this study. Although adenoviral infections are not as common in rodents as in humans, host immune responses may have been responsible for the lack of significant
NO tissue response after treatment with the iNOS labelled virus. However, the absence of a statistically different NO level between the dummy and iNOS labelled adenoviral treatment groups adds further support to the theory that iNOS is not the principle NO driving factor in the rat anal sphincter.

Our results have only demonstrated an increase in the tissue nitrate levels 21 days following treatment when compared to the control group sacrificed at 7 days. The significant result may have been secondary to the fall in the nitrate recorded in the control group, particularly as the day 21 iNOS nitrate levels were not significantly different from the control group nitrate levels. It is equally possible however that the finding is the result of a type II error. This is also the likely explanation for the significant difference between the day 21 dummy iNOS nitrate levels and the day 7 and overall control levels, particularly given the wide confidence interval range for the dummy iNOS group. [Fig 3] It may be however that the injury imposed with the injection genuinely increased tissue nitrate levels in both the dummy and iNOS labeled groups. The lack of difference between the dummy and iNOS nitrate levels would indicate that the iNOS was not the factor responsible for the nitrate increase.
2.4 The High Frequency Wave Form (Fast Wave) in the hypertonic internal anal sphincter: Validation of a new observation.

Abstract

Introduction: Slow wave (sw) and ultra-slow wave (usw) activity is sometimes observed in manometric traces of the hypertonic internal anal sphincter. A third wave form, first noted in anal fissure patients, is also present. The aim of this study was to validate the existence and consistency of that wave form.

Methods: The manometry traces of 60 anal fissure patients were recorded prospectively and analysed. The traces were then matched for age and gender with traces recorded from patients with either constipation or faecal incontinence on a pre-existing data-base. The remaining traces on the data-base (n=1067) were then reviewed and all traces with a maximum resting anal pressure (MRAP) greater than 89cmH$_2$0 (n=389) were analysed. An in vitro assessment of the effect on the wave form when pressures greater than 110cmH$_2$0 were applied to the manometry catheter was undertaken to exclude the possibility that the observed findings were the result of artefactual interference. Twenty patients demonstrating the fast wave activity on manometry had repeat manometry performed by an independent observer with continual cardiac monitoring.

Results: The Fast Wave (fw) only occurs at a maxRAP >110cmH$_2$0. The wave form has a frequency of 1-1.5 cycles per second (60-108 per minute) and has a maximum amplitude equivalent to 8.7% +/-2.91 (2SD) of the MRAP. In 74% of traces the fw occurs in the presence of either sw or usw activity. In 26% of traces the fw occurs in isolation. These findings were consistent irrespective of the indication for anorectal physiology testing. The fw was identified in 23% of all fissure traces. The wave was identified in 6% of the age and gender matched patients, all of whom there was a MRAP >130cmH$_2$0. From the remaining data-base fw were observed in 17% of the traces, 0/134 traces with a MRAP <110cmH$_2$0, 3/50 traces with a maxRAP 110-119cmH$_2$0, 4/50 traces
with a MRAP 120-129cmH₂O, 11/38 traces with a MRAP 130-139cmH₂O and 50/117 traces with a MRAP >139cmH₂O.
The wave form was reproducible at all pressure settings in the in vitro study. The manometric trace was reproduced on the control system and was not associated with cardiac activity.

**Interpretation:** The Fast Wave, identified only when the MRAP is >110cmH₂O, usually in the presence of either *sw* or *usw* activity, has a consistent frequency and predictable amplitude.
Introduction

Anorectal manometry is the standard method of investigation of the pressure and motility profiles of the anal sphincter. The smooth muscle internal sphincter is in a state of tonic partial contraction producing 85% of the anal resting pressure (Frenkner 1975). The remaining 15% of the anal resting pressure is formed by the external anal sphincter with a small contribution from the haemorrhoidal plexus (Sangwan 1998, Gutierrez 1975). Phasic variations in resting pressure, known as slow waves (sw), occur at a rate of 6-20 waves per minute with an amplitude of 10-25cmH₂O. Ultraslow waves (usw) occur at a frequency of 1-3 per minute and amplitude of 30-100cmH₂O and are observed in 5% of subjects with normal anal pressure but in up to 50% of cases when the pressure is above 100cmH₂O (Hancock 1976, Haynes 1982, Gibbons 1986) [Fig 1].

Using manometry (Penninckx 1992) and electromyography (Lubowski 1988, Farouk 1992) it has been demonstrated that these wave forms are generated by the internal anal sphincter (IAS). We have recently observed a third wave form, which we have called the fast wave, during a series of anorectal studies performed on patients with anal fissures. The purpose of this study was to define and validate this observation.
Methods

Sixty patients (28 female) with chronic anal fissure underwent anal manometry prior to commencing treatment. Studies were performed in the left lateral position with a six-channel, low compliance, side-hole, water perfusion system with computer acquisition and storage of data (Neomedix, Sydney, Australia). The most caudal recording port was positioned in the lower anal canal, so that five channels 0.75cm apart recorded anal canal pressure, and one (or more if the anal canal was short) recorded rectal pressure. Maximum anal resting pressure (MRAP) was measured once a stable baseline was established.

The resting pressures and wave form profiles were prospectively analysed. Slow wave and usw were defined by previously accepted parameters. IAS hypertonicity was defined as a maximum anal resting pressure greater than 110cmH\textsubscript{2}0 (Lubowski 1999, Read 1992). Manometric traces from the chronic fissure patients were then compared with traces taken from age and sex matched controls. The control subjects had a history of either faecal incontinence or constipation without a history of anal fissure. These traces were obtained from a pre-existing data base of 1187 subjects. Resting anal pressures and the wave form profiles were compared between the fissure group, the matched controls and a third group of subjects taken from the data base. In this last group, pressure profiles were analysed in groups of patients taking IAS pressure increments of 10cmH\textsubscript{2}0 using the highest recorded MRAP. Traces with a MRAP greater than 89cmH\textsubscript{2}0 were included, being those traces with a MRAP 20cmH\textsubscript{2}0 below the lowest MRAP where the fw was noted in the first two groups. This group consisted of a cohort of 389 subjects.

A bench-top study examining the effect of artificially induced high manometric pressures was then performed. Firstly graduated pressures from zero to 200cmH\textsubscript{2}0 were applied to individual side-holes along the silicon catheter. These pressures were then oscillated to examine the effect of rapid pressure changes on the manometric recording. The catheter was then incorporated into
a closed water filled system and the external pressure increased to predetermined levels as the trace was recorded.

Twenty patients with fast wave activity demonstrated on the Neomedix system and ten without consented to repeat anorectal manometry performed by an independent observer on an AcqKnowledge data acquisition system. This system records at a frequency of 300Hz compared with 20Hz for the Neomedix system. The independent observer was blinded as to which patients had demonstrated fast wave activity on the Neomedix system. During manometry all patients underwent cardiac monitoring. After five minutes of steady state recording the patients were requested to hold their breath for ten seconds. The fast wave rate was correlated both to pulse and respiratory rate.

The South Eastern Sydney Human Ethics Committee approved all protocols.

**Statistical Analysis**

The results were analysed using the Student's t-test. A \( p \) value <0.05 was considered statistically significant. Correlation coefficients were calculated with the Pearson's log rank coefficient.

**Results: [Table 1]**

**Fissure patients**

The maxRAP recorded from patients with anal fissures ranged from 64 to 251cmH\(_2\)O. Slow waves were noted in 42% of traces and usw in 43% of traces.
### Table 1: The frequency of sw, usw and fw activity dependent upon the MRAP.

<table>
<thead>
<tr>
<th>Fissure Patients</th>
<th>MRAP cmH₂O</th>
<th>No.</th>
<th>No. sw</th>
<th>No. usw</th>
<th>No. fw</th>
</tr>
</thead>
<tbody>
<tr>
<td>64-109</td>
<td>16</td>
<td>2</td>
<td>0</td>
<td></td>
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</tr>
<tr>
<td>110-119</td>
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<td>0</td>
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<tr>
<td>120-129</td>
<td>8</td>
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<td>1</td>
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</tr>
<tr>
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<tr>
<td>140-149</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>150-159</td>
<td>5</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>&gt;159</td>
<td>22</td>
<td>16</td>
<td>16</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>25(42%)</td>
<td>26(43%)</td>
<td>14(23%)</td>
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</tbody>
</table>

<table>
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<tr>
<th>Matched Controls</th>
<th>MRAP cmH₂O</th>
<th>No.</th>
<th>No. sw</th>
<th>No. usw</th>
<th>No. fw</th>
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<td>1</td>
<td>0</td>
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</tr>
<tr>
<td>&gt;159</td>
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<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>20(33%)</td>
<td>5(8%)</td>
<td>4(6%)</td>
<td></td>
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</tbody>
</table>

<table>
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<tr>
<th>Data Base</th>
<th>MRAP cmH₂O</th>
<th>No.</th>
<th>No. sw</th>
<th>No. usw</th>
<th>No. fw</th>
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<td>89-109</td>
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<td>50</td>
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<td>0</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>130-139</td>
<td>38</td>
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<td>4</td>
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<td>0</td>
</tr>
<tr>
<td>&gt;139</td>
<td>117</td>
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<td>28</td>
<td>50</td>
<td>0</td>
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<tr>
<td>Total</td>
<td>389</td>
<td>39(10%)</td>
<td>32(8%)</td>
<td>68(17%)</td>
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</tr>
</tbody>
</table>

The presence of *sw* or *usw* activity positively correlated with the recorded MRAP (*p*<0.03). A third wave form, the *fw*, was noted in 23% of the traces. Each of these traces had a MRAP greater than 140cmH₂0 (141-215cmH₂0).

This newly identified wave form had a frequency of 60-108 waves per minute and amplitude of 7-28cmH₂0 (mean 14cmH₂0). The wave amplitude was dependent upon the MRAP and varied from 3 to 11% of the MRAP. The wave form was identified in the mid and lower anal canal only. In 76% of the traces the wave occurred in the presence of either *sw* or *usw* activity. In 54% of the traces in which the *fw* was identified all three wave forms were present [Figure 1, Figure 2].
Fig 2: Manometric trace, channels 1.5cm, 2.25cm, 3.0cm from anal verge demonstrating slow wave, ultraslow wave and fast wave activity. MRAP of 215cmH$_2$O

Fig 3: manometric trace, rectal, 3.75cm, 3.0cm, 2.25cm and 1.5cm from anal verge. MRAP 215cmH$_2$O. fw activity - frequency 90/min, amplitude 15-34cmH$_2$O
Matched Controls

The MRAP of the 60 age- and gender-matched controls ranged from 43-185cmH\textsubscript{2}O. Slow wave and usw activity was noted in 33% and 8% of traces respectively. The presence of these wave forms did not correlate with the MRAP. The fw was noted in 6% of the traces. Each of these traces had a MRAP greater than 130cmH\textsubscript{2}O (134-178 cmH\textsubscript{2}O). The wave frequency was 81 to 99 waves per minute. The wave amplitude was 7 to 12% of the MRAP or 8-11cmH\textsubscript{2}O (mean 9cmH\textsubscript{2}O). The wave form was identified in the mid to lower anal canal only. Slow or usw activity was present in all traces in which the fw was also recorded. There were an insufficient number of traces in which the fw was identified to allow statistical comparison with the wave form identified in the anal fissure manometry traces.

Data-base patients

The MRAP of the traces taken from the remaining data-base (n=389) ranged from 89 to 250cmH\textsubscript{2}O. Slow wave and usw activity was noted in 10 and 8% respectively. The presence of the usw and sw activity positively correlated with a higher MRAP. The fw was noted in 17% of the traces. The wave frequency was 60 to 102 waves per minute. The wave amplitude was 3 to 14% of the MRAP or 5-30 cmH\textsubscript{2}O (mean12 cmH\textsubscript{2}O). The fw was identified only in the mid to lower anal canal. The fw occurred in the presence of usw or sw activity in 74% of traces. The fw parameters were not significantly different from the fw parameters identified in the anal fissure manometry traces (p=0.33 for frequency and p=0.32 for amplitude).

Bench study

The manometric pressure recording promptly responded to changes in the pressure applied to the side-hole of the silicone catheter and to the catheter within the closed system. Gradations of 5cmH\textsubscript{2}O were clearly demonstrated. With the application of a constant pressure even at levels of 200cmH\textsubscript{2}O there was no fluctuation in the pressure recorded. There was no evidence of fast-
wave, slow wave or ultra-slow wave activity irrespective of the pressure
constantly applied. Oscillation of the pressure at a frequency of one to two
cycles per second replicated the fast wave activity seen in the hypertonic
sphincter. These oscillations were producible within any pressure gradient.

**Independent Observer Manometry with Cardiac Monitoring**

There was 100 percent concordance between the Neomedix and
AcqKnowledge systems for the demonstration of fast wave activity. The median
pulse rate was 65 beats per minute. There was no significant correlation
between the fast wave frequency and the pulse rate for the individual patient
\[ p = 0.984 \]. Nor did the fast wave rate vary dependent upon respiration.

**Discussion**

Slow waves and ultra-slow waves have been recognised as an integral part of
the phasic internal sphincter activity. They occur more frequently in the distal
anal canal (Keck 1995), and are more common in the presence of a hypertonic
IAS (Hancock 1975). It has therefore been postulated that they occur as a result
of abnormal IAS contractions (Hancock 1977, McNamara 1990). Our results
confirm an increase in the frequency of the \( sw \) and \( usw \) activity in the hypertonic
fissure. The \( fw \) was initially observed during a series of these traces.

The \( fw \) was identified in 6-23\% of traces across all three groups of traces
analysed. The presence of the \( fw \) was dependent on the MRAP to an even
greater extent than the \( sw \) or \( usw \). The \( fw \) was not identified in any trace with a
MRAP less than 110cmH\(_2\)O. It had a clearly defined frequency of 60-108 per
minute, three to five times greater than the \( sw \). The \( fw \) also had an amplitude
within a clearly defined range of 5-30cmH\(_2\)O. The amplitude positively
correlated with the recorded MRAP. As previously reported for \( sw \) and \( usw \)
activity, the \( fw \) was observed in the mid to distal anal canal (Hancock 1977).
Parameters for all three wave forms are summarized in Table 2.
Table 2: Manometric phasic wave form parameters

<table>
<thead>
<tr>
<th></th>
<th>sw</th>
<th>usw</th>
<th>fw</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRAP/cmH\textsubscript{2}O</td>
<td>not defined</td>
<td>not defined</td>
<td>&gt;110</td>
</tr>
<tr>
<td>frequency/min</td>
<td>10-20</td>
<td>1-3</td>
<td>60-108</td>
</tr>
<tr>
<td>amplitude /cmH\textsubscript{2}O</td>
<td>10-25</td>
<td>30-100</td>
<td>5-30</td>
</tr>
</tbody>
</table>

The effect that variations in the diameter of the manometry catheter and the rate of perfusion in the water-perfused system may have on the recorded wave form and maximum pressures is well documented (Gutierrez 1975, Hill 1960). The low compliance, six side-hole perfusion system used in this study has been previously shown to be an accurate and reproducible system for recording IAS contractions and for eliciting a rapid response to IAS pressure changes (Taylor 1984). In this study all traces including those in the study as well as those collected in the database during the preceding five years were recorded in a standardised manner by one person (MLK). Technical errors are unlikely to be responsible for the motility pattern observed.

Although the ideal control group would have been normal patients the study group did provide its own internal control in that 230 of the 326 traces with a maxRAP>110 cmH\textsubscript{2}O did not exhibit fast wave activity. However, the in vitro analysis was performed to confirm that the wave form observed was not secondary to artefactual interference consequent upon the high pressure being measured. The fast wave was reproducible with oscillations of the pressure applied at any given pressure baseline. Proportionately equivalent variations in MRAP are more likely to be detected at a higher MRAP because of the greater absolute amplitude change. However, this was not the case in the in vitro study. Effecting an 8% measurable oscillation in the pressure became technically more challenging as the baseline pressure diminished but the wave form produced was consistent. This finding confirms that the measured changes are true oscillating changes in the resting pressure of the internal anal sphincter as the trace progresses. In vivo, the documented oscillation in resting pressure only occurs when the resting anal pressure is greater than 110 cmH\textsubscript{2}O. Only the hypertonic internal anal sphincter demonstrates fast wave contraction similar to skeletal muscle tetany.
The significance of the \textit{fw} remains to be determined. The presence of the \textit{fw} is not disease specific but is dependent upon the MRAP. In line with earlier interpretations of \textit{sw} or \textit{usw} activity, the presence of these waves in 76\% of the traces in which the \textit{fw} was identified might support an abnormality of IAS motility (Hancock 1977, McNamara 1990), although since \textit{sw} and \textit{usw} are observed in normal asymptomatic subjects, these waves as well as the \textit{fw} may simply reflect a high sphincter pressure \textit{per se}. However, the total absence of the \textit{fw} at MRAP less than 110cmH\textsubscript{2}O and the results of our in vitro assessment would suggest that the wave form does reflect something of physiological significance. Internal sphincter electromyography in various disease states may shed further light on this.

The potential therapeutic implications of eliminating IAS tetany is demonstrated by the experience of the biliary physicians. Variations in the motility pattern dependent upon the basal Sphincter of Oddi pressure have been identified. The hypertonic or dysfunctional sphincter of Oddi (SOD) has a high resting pressure and increased frequency, amplitude and duration of phasic high pressure contractions (Sherman 2001). Although the basal sphincter pressure is currently the only parameter of diagnostic significance for SOD, endoscopic neurochemical treatment has resulted in the dissipation of the increased phasic contractions and resolution of disease symptoms for the duration of the treatment (Wehrmann 1998). Hancock reported in 1977 reported similar findings in the manometric traces of anal fissure patients treated with lateral sphincterotomy (Hancock 1977). Surgical intervention resulted in a reduction in the \textit{usw} activity. However, there has been no further comment on the effect of a variety of treatments, including nitrates (Kennedy 1999, Altomare 2000), nifedipine (Antropoli 1999) and botulinum toxin (Minguez 1999, Maria 1998) on the manometric wave-form. Ten percent of the IAS pressure generated is myogenic in origin and 45\% is neurogenic (Sangwan 1998). Either source may be responsible for the augmented IAS activity and may therefore be potential sites of therapeutic intervention. The effect of neurochemical IAS modulation on the manometric motility pattern requires further investigation.
Conclusion

A new phasic wave form, the fast wave, has been observed in the hypertonic IAS. This complements the known two phasic wave forms, the sw and usw, which have been previously defined as normal variations in internal anal sphincter tone. This study defines the manometric parameters of the fast wave. The clinical significance and potential therapeutic implications of the fw have yet to be investigated.
CHAPTER 3

ANAL INCONTINENCE

3.1 Faecal Incontinence: a multifactorial problem
[Accepted for publication as Thornton MJ, Kennedy ML, Lubowski DZ. Faecal incontinence: a multifactorial problem. Colorectal Disease 2005].

3.2 Long-term follow-up of dynamic graciloplasty for faecal incontinence

3.3 Re-do anal sphincter repair

3.4 Extracorporeal magnetic stimulation of the pelvic floor; impact on anorectal function and physiology. A pilot study
[Accepted for publication as Thornton MJ, Kennedy ML, Lubowski DZ. Extracorporeal magnetic stimulation of the pelvic floor; impact on anorectal function and physiology. A Pilot study. DCR 2005;48:00-00]

3.5 Long-term indwelling seton for complex anal fistulae in Crohn’s disease
3.1 Faecal Incontinence: a multifactorial problem

Abstract

Aim: To investigate the interplay of gender, age, parity, birth injury, hysterectomy and perineal surgery on pelvic floor function and physiology.

Methods: A retrospective analysis of prospectively collected data was performed. One thousand and fifty-five patients underwent anorectal physiology and completed a questionnaire assessing bowel symptoms, obstetric and surgical history. Vienna constipation and Wexner incontinence scores were also completed. Pudendal nerve terminal motor latency (PNTML) was performed in 716 of these patients. Balloon sensitivity testing was performed in 386 patients. Endoanal ultrasound was performed in 502 patients. Data was analysed with stepwise logistic regression to assess those factors significantly associated with the symptom of faecal incontinence and each physiological parameter assessed.

Results: Assessment of the symptom of faecal incontinence, with linear regression analysis found increasing age, female gender and history of a birthing injury to be significant. Increasing age, female gender and birth injury were also significant for lower anal resting and squeeze pressures. Female gender and birth injury were significant for reduced cough pressures and maximum tolerated balloon volumes. Birth injury alone was significant for lower urge balloon volumes and age only was significant for prolonged PNTML and reduced anal electrosensitivity. Previous anal surgery and birth injury were significant for the presence of ultrasound detected internal anal sphincter defects. Age only was significant for the presence of external anal sphincter defects. [Each were significant to p<0.001]

Conclusion: There are significant anorectal physiology differences dependent upon the age, gender and presenting colorectal symptom. However controlling for age and gender identified birth injury as the single dominant factor in
association with poorer physiology and ultrasound results and higher faecal incontinence scores.
Introduction

The aetiology of faecal incontinence continues to be debated (Jorge 1993, Vaizey 1997, Donnelly 1998). Cross-sectional and intermediate-term prospective studies suggest significant associations between faecal incontinence and increasing age, female gender and increasing parity (Bannister 1997, Lam 1999, Sun 1989, Abramowitz 2000). Age, gender and parity are also associated with significant changes in anorectal physiology (Jameson 1994, Ryhammer 1997). Their relative roles however are a little less clearly defined. On multivariate analysis parity may not be significant (McHugh 1987). The effect of hysterectomy long-term is also poorly defined although in the short-term, function and anorectal physiology appear to be unchanged (Goffeng 1997, Prior 1992). Birth injury has been shown to be significantly associated with the presence of anal sphincter defects on ultrasound and the development of post-partum faecal incontinence (Abramowitz 2000, Zetterstrom 1999, Reiger 1998). There have been no studies assessing the impact of a birth injury on anorectal physiology in the longer-term. There have however been several pieces of legislation that imply that birthing injuries are not a significant concern.

In 1998 the Senate Inquiry "Rocking the Cradle - A Report Into Childbirth Procedures" recommended that the Commonwealth Government work with the State Governments to ensure that comprehensive and objective information concerning birth options be available to all pregnant women. Like other reports into childbirth, this report focused on infant and maternal mortality and caesarean section rates as the prime outcome measures of safe birthing. The report concluded that “Childbirth in Australia is safe for mothers and babies. Preventable adverse outcomes are rare and decreasing.’

Contrary to their conclusion in New South Wales in 2000, 4.3% of women, 2495 in total, were reported to have clinically detected 3rd or 4th degree obstetric tears (New South Wales Mothers and Babies Report). Given that only three percent of tears are clinically detected 25,527 women in New South Wales in 2000 will have had a sphincter injury resulting from vaginal delivery (Sultan 1993).
significant number of these women will develop symptoms of faecal or urinary incontinence (Abramowitz 2000, Zetterstrom 1999, Reiger 1998).

In attempt to clarify the relative role of birthing injury this study assesses the impact of age, gender, parity, hysterectomy and birthing injury on anorectal symptoms, anorectal physiology and endo-anal ultrasound.

**Methods:**

Between June 1998 and April 2003, 1119 patients attended the anorectal physiology laboratory. Of these, 1055 patients prospectively completed a questionnaire which included age, gender, obstetric history, pelvic surgery history, a Wexner continence score, a Vienna constipation score and age of symptom onset. They then underwent anorectal physiology including resting, squeeze and cough pressures. The physiology was performed with a stationary water perfused, side-hole catheter analysed through a Neomedix computer data storage system. Of these patients, 716 also underwent PNTML testing using a St Marks electrode and anal mucosal electrosensitivity testing using a urethral ring electrode. Of the 1055 with a complete history and physiology, 386 also underwent balloon sensitivity and capacitance testing. In this a silastic balloon is attached to the end of the manometry catheter and gradually filled with air. The patients report first rectal sensation, first urge to empty and maximum tolerable urge. The balloon volume at each point is recorded.

Five hundred and two patients had a concomitant anorectal ultrasound documenting the presence of sphincter defects. This was performed with a 7.5Hz linear probe [Aloka]. The sphincter is assessed circumferentially and images recorded from one to twelve o’clock.

All data was collected by a single observer prior to the inception of the analysis.

The physiology and ultrasound results and presenting symptoms were compared firstly across all patients to assess the impact of gender, age at testing and previous pelvic surgery. The females only were then analysed
independently to assess the impact of parity, birth injury and hysterectomy as well as the above factors.

**Statistical Analysis**

A two sample t-test was used for continuously scaled data. Chi-squared was used for analysis of nominal data. Multi-group analysis was assessed with ANOVA. A p value <0.05 was considered significant (two-tailed). Linear stepwise regression was performed with SPSS statistical software [SPSS Ltd, version 11, Chicago, Illinois, USA].

**Results**

One thousand and fifty-five patients were eligible for inclusion (816 female). The mean age at testing was 58.15±16.2 years. Five hundred and twenty-six were over 60 years of age. Seven hundred and thirty-one patients reported symptoms of faecal incontinence. Two hundred and seventy-five patients had undergone anal surgery and a further 34 had undergone previous pelvic surgery. Table 1 summarises the significant risk factors and anorectal physiology differences for gender, age and bowel symptoms. Six hundred and ninety-eight women had had a full-term vaginal delivery. The median number of children was 2 (range 0-8). The median interval from vaginal delivery was 24 years (range 0-57 years). Women with two or more deliveries had significantly higher hysterectomy rates (p<0.001, OR 3.28). Anal surgery rates also increased with parity from 14 percent (16/113) in the nulliparous group to 32 percent (19/60) in those women with five or more deliveries (p=0.01).

Of the parous women 66 percent (463/698) reported a perineal intervention at the time of delivery. [Table 2] The birth injury rate continued to increase from the first to the third vaginal delivery but not thereafter (p=0.001)
<table>
<thead>
<tr>
<th></th>
<th>male</th>
<th>Female</th>
<th>p</th>
<th>&lt;60</th>
<th>&gt;60</th>
<th>P</th>
<th>Const.</th>
<th>Fl</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max RAP (cmH₂O)</td>
<td>95.1±37</td>
<td>77.9±36</td>
<td>.000</td>
<td>95.1±39</td>
<td>68.5±33</td>
<td>.000</td>
<td>105.3±39</td>
<td>72.2±34</td>
<td>.000</td>
</tr>
<tr>
<td>Mean RAP (cmH₂O)</td>
<td>67.7±28</td>
<td>50.9±25</td>
<td>.000</td>
<td>62.5±27</td>
<td>46.9±23</td>
<td>.000</td>
<td>69.5±28</td>
<td>48.5±24</td>
<td>.000</td>
</tr>
<tr>
<td>Squeeze (cmH₂O)</td>
<td>163.4±61</td>
<td>84.7±57</td>
<td>.000</td>
<td>107.6±63</td>
<td>97.1±69</td>
<td>.011</td>
<td>121.7±59</td>
<td>94.3±68</td>
<td>.000</td>
</tr>
<tr>
<td>Cough (cmH₂O)</td>
<td>142.1±48</td>
<td>94.7±39</td>
<td>.000</td>
<td>103.5±43</td>
<td>107.3±48</td>
<td>.184</td>
<td>112±44</td>
<td>102.2±46</td>
<td>.002</td>
</tr>
<tr>
<td>1st sensation (mls)</td>
<td>37.1±14</td>
<td>36.2±18</td>
<td>.615</td>
<td>36.7±20</td>
<td>36.1±9</td>
<td>.728</td>
<td>36.7±16</td>
<td>35.3±11</td>
<td>.347</td>
</tr>
<tr>
<td>Urge volume (mls)</td>
<td>114.1±55</td>
<td>104.2±52</td>
<td>.092</td>
<td>110.2±60</td>
<td>102.7±41</td>
<td>.177</td>
<td>116.9±62</td>
<td>98.8±40</td>
<td>.001</td>
</tr>
<tr>
<td>Maximum urge volume (mls)</td>
<td>184.7±84</td>
<td>163.2±77</td>
<td>.014</td>
<td>172±85</td>
<td>166.3±70</td>
<td>.492</td>
<td>183.6±86</td>
<td>158.8±69</td>
<td>.002</td>
</tr>
<tr>
<td>Left pudendal (mHz)</td>
<td>2.05±0.28</td>
<td>2.12±0.32</td>
<td>.083</td>
<td>2.04±0.29</td>
<td>2.17±0.3</td>
<td>.000</td>
<td>2.09±0.3</td>
<td>2.12±0.3</td>
<td>.344</td>
</tr>
<tr>
<td>Right pudendal (mHz)</td>
<td>2.04±0.33</td>
<td>2.1±0.33</td>
<td>.101</td>
<td>2.03±0.29</td>
<td>2.15±0.3</td>
<td>.000</td>
<td>2.04±0.29</td>
<td>2.11±0.3</td>
<td>.031</td>
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<tr>
<td>Rectal sensitivity (mHz)</td>
<td>6.82±3</td>
<td>7.19±3.86</td>
<td>.319</td>
<td>6.29±2.82</td>
<td>7.79±4.2</td>
<td>.000</td>
<td>6.44±2.8</td>
<td>7.3±3.92</td>
<td>.19</td>
</tr>
<tr>
<td>Age at symptom onset</td>
<td>54.7±18</td>
<td>52.4±19</td>
<td>.087</td>
<td>39.1±13</td>
<td>66.7±12</td>
<td>.000</td>
<td>41.5±19</td>
<td>57.7±17</td>
<td>.000</td>
</tr>
<tr>
<td>IAS defect (present)</td>
<td>26/50</td>
<td>166/452</td>
<td>.035</td>
<td>85/211</td>
<td>107/291</td>
<td>.424</td>
<td>OR .86</td>
<td>12/45</td>
<td>.09</td>
</tr>
<tr>
<td>EAS defect (present)</td>
<td>6/48</td>
<td>68/446</td>
<td>.612</td>
<td>45/206</td>
<td>29/288</td>
<td>.000</td>
<td>OR .4</td>
<td>7/45</td>
<td>.96</td>
</tr>
<tr>
<td>Urinary incontinence (yes)</td>
<td>2/237</td>
<td>326/816</td>
<td>.001</td>
<td>66.5</td>
<td>143/529</td>
<td>185/526</td>
<td>.004</td>
<td>OR 1.47</td>
<td>51/289</td>
</tr>
<tr>
<td>Previous surgery (yes)</td>
<td>86/239</td>
<td>189/816</td>
<td>.001</td>
<td>154/529</td>
<td>155/526</td>
<td>.096</td>
<td>OR 1.02</td>
<td>96/289</td>
<td>.155</td>
</tr>
<tr>
<td>Faecal Incontinence</td>
<td>155/225</td>
<td>576/795</td>
<td>.019</td>
<td>OR 2.38</td>
<td>295/529</td>
<td>436/526</td>
<td>.000</td>
<td>OR 3.83</td>
<td>Na</td>
</tr>
</tbody>
</table>

Table 1: All patients, n=1055, values given are the mean± STD deviation. OR = Odds ratio. Odds ratio is expressed for the right hand of the two outcome factors. [Const.=constipation, Fl= faecal incontinence.]
 Forty-two percent (346) of women had undergone a hysterectomy prior to testing. While hysterectomy rates were increased in both parous women and those with a birth injury, parity alone was significant on regression analysis. Table 3 summarises the significant risk factors and anorectal physiology differences for parity, birth injury and hysterectomy.

### Differences dependent upon presenting bowel symptoms

Two hundred and ninety patients were referred with symptoms of constipation, 731 with faecal incontinence and 34 for other reasons including pre-operative assessment before ultra-low anterior resection or reversal of Hartmanns. There was a statistically significant association between a referral diagnosis of faecal incontinence and a high incontinence score and a low evacuation score. A referral diagnosis of incontinence also positively correlated with a lower MRAP (p<0.001 for all).

Those patients with constipation presented at a significantly younger age than those with faecal incontinence (p<0.001). Differences in previous surgery rates were not significant (p=0.079). Although there was an equal distribution of nulliparous women in both groups, there were significantly more multiparous women in the incontinent group (p<0.001, OR 2.17). The percentage of the women presenting with faecal incontinence increased from 51% (52/107) in the nulliparous group to 84% (36/43) in those with five vaginal deliveries (p<0.001). Significantly more women in the incontinent group had also experienced a birth injury (p<0.001, OR 1.85) or had undergone a hysterectomy (p<0.001, OR 1.8).
The incidence of urinary dysfunction was also significantly greater in the faecal incontinent cohort (p<0.001, OR 3.14).

Logistic regression identified age and birth injury to be independent factors in the development of faecal incontinence (p<0.001).

<table>
<thead>
<tr>
<th>Parity</th>
<th>P</th>
<th>Birth injury</th>
<th>P</th>
<th>Hyster.</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1 n=194</td>
<td>&gt;1 n=621</td>
<td>Yes n = 443</td>
<td>No n = 373</td>
<td>Yes n=346</td>
<td>No n=470</td>
</tr>
<tr>
<td>Max RAP (cmH2O)</td>
<td>6.4±4.3</td>
<td>75.4±36</td>
<td>0.001</td>
<td>73.4±36</td>
<td>81±41</td>
</tr>
<tr>
<td>Mean RAP (cmH2O)</td>
<td>95.5±67</td>
<td>81.4±57</td>
<td>0.002</td>
<td>48.9±23</td>
<td>35.4±27</td>
</tr>
<tr>
<td>Squeeze (cmH2O)</td>
<td>95.5±67</td>
<td>81.4±57</td>
<td>0.003</td>
<td>77.3±53</td>
<td>93.6±60</td>
</tr>
<tr>
<td>Cough (cmH2O)</td>
<td>99.9±41</td>
<td>93.1±39</td>
<td>0.033</td>
<td>91.4±38</td>
<td>98.7±40</td>
</tr>
<tr>
<td>T1 sensation (m/s)</td>
<td>38.2±21</td>
<td>35.3±16</td>
<td>0.212</td>
<td>35.1±16</td>
<td>37.1±19</td>
</tr>
<tr>
<td>Urge volume (m/s)</td>
<td>116.5±6</td>
<td>99.2±47</td>
<td>0.013</td>
<td>96.9±43</td>
<td>110.9±58</td>
</tr>
<tr>
<td>Max volume (m/s)</td>
<td>181.6±64</td>
<td>155.7±72</td>
<td>0.012</td>
<td>153.1±68</td>
<td>172.3±83</td>
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<td>Left pudendal (mHz)</td>
<td>2.1±0.31</td>
<td>2.13±0.33</td>
<td>0.488</td>
<td>2.11±0.32</td>
<td>2.14±0.32</td>
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<tr>
<td>Right pudendal (mHz)</td>
<td>2.09±0.32</td>
<td>2.11±0.33</td>
<td>0.532</td>
<td>2.1±0.34</td>
<td>2.11±0.32</td>
</tr>
<tr>
<td>Rectal sensitivity (mHz)</td>
<td>6.7±2.35</td>
<td>7.3±4.13</td>
<td>0.110</td>
<td>7.22±3.56</td>
<td>7.17±4.22</td>
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<td>Ias defect</td>
<td>25/69</td>
<td>140/382</td>
<td>0.412</td>
<td>118/277</td>
<td>48/175</td>
</tr>
<tr>
<td>Eas defect</td>
<td>8/68</td>
<td>60/377</td>
<td>0.622</td>
<td>50/272</td>
<td>18/174</td>
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<tr>
<td>Age symptom onset</td>
<td>46.1±22</td>
<td>54.3±37</td>
<td>0.000</td>
<td>52.5±17</td>
<td>52.3±21</td>
</tr>
<tr>
<td>Urinary incont. (yes)</td>
<td>51</td>
<td>275</td>
<td>0.000</td>
<td>205</td>
<td>121</td>
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<td>Hyster. (yes)</td>
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<td>140</td>
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<tr>
<td>Parity &gt;1</td>
<td>Na</td>
<td>na</td>
<td>Na</td>
<td>395</td>
<td>226</td>
</tr>
<tr>
<td>Birth injury (yes)</td>
<td>48</td>
<td>395</td>
<td>0.000</td>
<td>Na</td>
<td>Na</td>
</tr>
<tr>
<td>Faecal incont.</td>
<td>111</td>
<td>464</td>
<td>0.000</td>
<td>337</td>
<td>239</td>
</tr>
</tbody>
</table>

Table 3: All women n= 816, OR = Odds ratio. Odds ratio expressed for parous women, women with a birth injury and a hysterectomy.
Comparing physiology on the basis of a presenting symptom identified significant differences in the maximum, mean, squeeze and cough pressures (p<0.002 for all). The urge and maximum tolerated volumes with balloon testing were also significantly greater in the constipated group (p=0.001,p=0.002 respectively). The internal and external anal sphincter defects detected were not significantly different (0.09, 0.963). There were however, significantly more women with internal anal sphincter defects in the faecal incontinence cohort (p=0.034, OR 1.77). The PTNML was also prolonged and the anal mucosal electrosensitivity increased in women with faecal incontinence (p=0.005, p=0.017 respectively).

**Differences dependent upon age of symptom onset**

Three factors significantly impacted on the age of symptom onset. Nulliparous women presented at a younger age (p<0.001). Patients with constipation presented at a younger age (p<0.001) and those not having had a hysterectomy presented at a younger age (p<0.001). All three factors were significant on linear regression analysis.

**Physiology**

An assessment of each component of physiology and ultrasound for differences dependent on the presence of a known risk factor for pelvic floor dysfunction identified the following.

Maximum resting and mean resting anal pressures were significantly reduced if female (p<0.001) and in those over 60 years of age (p<0.001). There was a significant negative linear association between age in decades and MRAP (p<0.001). [Figure 1]
MRAP was also significantly reduced in the presence of a prior hysterectomy (0.003, 0.004), three or more vaginal deliveries (0.000) and any birth injury (0.001). The MRAP documented in those giving a history of forceps, tear or episiotomy were all significantly lower than those without such a history (p=0.003, 0.000). [Figure 2]
MRAP was also significantly reduced in the presence of either an internal or external anal sphincter injury imaged on ultrasound. On linear regression analysis of the entire cohort patient age at testing and gender were independently significant (p<0.001 both). Linear regression of the female cohort found age at testing and birth injury to be independently significant (p<0.001 both).

Squeeze pressure was significantly reduced in females (p<0.001) and in those over 60 years of age (p<0.001). Again there was a negative linear association between age in decades and squeeze pressure. Squeeze was also reduced in the presence of previous anal surgery (p=0.037). Linear regression analysis again found age at testing and gender to be independently significant (p<0.001). In the female cohort squeeze was also reduced in the presence of a previous birth injury and hysterectomy (0.000, 0.001). The squeeze pressures were reduced irrespective of whether the birth injury was forceps, perineal tear or episiotomy (p=0.002, 0.043, 0.002 respectively). Squeeze pressures were also significantly lower in those with five or more deliveries (p=0.015). Age and birth injury were independently significant on linear regression analysis (p<0.001).

Cough pressures were significantly lower in women (p<0.001) but were not age dependent. They were also reduced in the presence of previous surgery. Linear regression analysis found gender and previous surgery to be independently significant (p<0.001). In the female cohort reduced cough pressure were also documented in the presence of two or more deliveries (p=0.022), a previous birth injury (0.007) and previous anal surgery (0.048). The reduction in cough pressure in the presence of a birth injury was irrespective of the type of injury (p<0.001 for all). In the female only cohort birth injury was the only independently significant variable on linear regression analysis (p=0.006).

First sensation with rectal balloon testing was not significantly affected by any factor.
Urge volumes on balloon testing were not affected by age or gender. In the female cohort however the urge volume was significantly decreased following a birth injury \( (p=0.027) \). In particular it was decreased following a tear or episiotomy \( (p=0.05) \). Birth injury remained significant on linear regression analysis \( (p=0.03) \).

Maximum tolerated balloon volumes were significantly reduced in women \( (p=0.014) \). In the female cohort maximum tolerated volumes were reduced following birth injury \( (p=0.04) \), specifically associated with the use of forceps \( (p=0.037) \). Birth injury was the only significant factor on linear regression analysis of maximum tolerated volumes \( (p=0.038) \).

PTNML significantly increased with increasing age \( (p<0.001) \) [Figure 3]. The left and right measurement did not significantly differ \( (p<0.001) \). Although the PNTML latencies did not significantly differ dependent upon parity, parity and PNTML had a statistically significant positive correlation \( (p=0.03) \). Age was the only significant variable on linear regression analysis for all patients and the female cohort \( (p<0.001) \).

Figure 3: Pudendal Nerve Terminal Motor Latency (PNTML/mHz) across age groups in decades. (Bars = mean ±2SD)
Anal mucosal sensitivity significantly reduced with age and following pelvic surgery (p<0.001, p=0.006 respectively). Both were independently significant on regression analysis (p<0.001 both). In the female cohort rectal sensation negatively correlated with parity (p=0.001) and positively correlated with PNTML (p=0.001) such that as parity increased mucosal sensitivity decreased and PNTML increased. As with PNTML however, anal mucosal electrosensitivity did not significantly differ between the parous and nulliparous groups. Anal mucosal electrosensitivity also increased with increased age at testing and previous pelvic surgery in the female cohort. On linear regression analysis age, surgery and parity were all independently significant (p<0.001 all).

Internal anal sphincter defects were more common in men and in association with previous pelvic surgery (p<0.001). Both were significant on linear regression analysis. In the female cohort, hysterectomy and a birth injury were also significant (p<0.001). The frequency of internal sphincter defects increased from 29% (49/122) in those without a reported injury to 50% (18/36) of those reporting a tear and 45% (73/162) of those reporting a forceps assisted delivery (p=0.019). Those having had a hysterectomy had lower rates of sphincter defects on ultrasound (p=0.04). Linear regression analysis identified birth injury and previous surgery to be significant (p<0.001 for both).

External anal sphincter defects were associated younger age at testing and previous pelvic surgery. Linear regression identified age at testing as the only significant variable (p=0.001). In the female cohort external anal sphincter injury was also associated with a previous birth injury, in particular a perineal tear. However on linear regression, age at testing was the only independent factor of significance (p=0.001).

**Discussion**

Several publications support our findings that men have more favourable anorectal physiology results (Bannister 1997, Sun 1989, Jameson 1994). The increased rate of internal anal sphincter defects in men was unexpected and
although partly explained by the increased rate of anal surgery the cohort is likely not to be representative of the general population. However currently there are no studies assessing the rate of occult sphincter defects in men.

Increasing age has also been shown to have a negative linear association with resting, squeeze and rectal filling pressures (Jameson 1994, Ryhammer 1997). In this study, age was a significant covariant for many physiological parameters. While this is likely to represent a genuine difference, from the data-base we were not able to control for many of the differences inherent in the age differences. Differences such as medication, co-morbidity and obesity may have had a significant impact. We were also not able to control for menopausal status. Ryhammer et al suggested that the greatest physiological differences were following menopause, rather than following a specific age cohort (Ryhammer 1997). Ryhammer et al did however report a direct association with age independent of menopause status.

Several studies report a reduction in resting and squeeze pressures immediately post-partum in both symptomatic and asymptomatic women (Abramowitz 2000, Reiger 1998, Hojberg 2003). In the longer-term, the literature would suggest that while there may be a trend toward a reduction in pressure, this is not significant (Ryhammer 1996). Consistent with our results McHugh et al found that on multivariate analysis all of the reduction seen longer-term was accounted for by age (McHugh 1987). As reported by Ryhammer et al, we also found a linear association between symptoms of faecal incontinence and increased parity (Ryhammer 1995). However, again on linear regression analysis parity was not independently significant. We did not identify a significant association between parity and PNTML as suggested by previous authors (Ryhammer 1996, Snooks 1990, Fynes 1999). However, this may reflect the reproducibility of the test rather than a true absence of pelvic nerve denervation in association with parity, particularly as there was a significant decrease in squeeze and cough pressures with increasing parity (Lubowski 1988). Our comparative groups did not include a cohort with normal colorectal function. This design flaw prevents extrapolation of incidence and
prevalence figures to the general population. It does not prevent identification of factors which may predispose to colorectal symptoms.

The symptomatic and physiological effects of birthing injuries continues to be debated. While the literature suggests that 25-50% (Reiger 1998, Wood 1998) of women with an ultrasound detected sphincter injury will be symptomatic, only 45% of women with post-partum faecal incontinence will have a sphincter defect on ultrasound (Abramowitz 2000). Symptoms of faecal incontinence in women have been shown to be positively associated with delivery of the first child, forceps, perineal tears, episiotomy and large birth weight babies (Zetterstrom 1999, Handa 2001). These factors have also been shown to be associated with the presence of an ultrasound detected sphincter defect. We did not assess neonatal birth weight but found the other factors to be independently significant for symptoms of faecal incontinence. To the author’s knowledge no paper has previously assessed the physiological impact long-term of obstetric birth injuries.

On linear regression analysis, birth injury was independently significant for lower MRAP, squeeze and cough pressures, urge and maximum tolerated rectal balloon volumes. Furthermore, significant changes were seen following forceps, tear, episiotomy or a combination injury. Resting pressure was significantly reduced following forceps and episiotomy or tear. Squeeze and cough pressures were reduced following any of the injuries assessed. Rectal sensation and balloon urge volumes were significantly lowered following a tear or episiotomy and maximum tolerated volumes were significantly lower following a forceps delivery. Birth injuries have been shown to have an adverse effect on anorectal function which is statistically independent of the effects of age, parity, hysterectomy and pelvic surgery. Further research is warranted to address the long-term effects on anorectal function of this potentially preventable injury.

Our birth injury findings could be criticised on the basis that the obstetric data was collected retrospectively. While a longitudinal prospective study would be ideal the resources required would be great. We believe however that our data
is reliable. Firstly, the frequency of ultrasound detected anal sphincter defects in the female cohort was in keeping with that expected from the literature (Abramowitz 2000, Wood 1998). There was also a positive association between a birth injury and the presence of an ultrasound defect. Secondly, although there are no publications supporting the accuracy of maternal recollection of major birthing events, few women in our experience report that they do not remember whether forceps were used or a tear or episiotomy occurred during the delivery. Women who were unsure of their obstetric history were not included in the study cohort.

Despite the association between faecal and urinary incontinence (Meshia 2002, Manning 2001), unlike in urinary incontinence (Milsom 1993, Brown 2000), an association between hysterectomy and a physiological deterioration in anorectal function has not been proven (Prior 1992). Although we report an increase in faecal incontinence in those patients having had a hysterectomy, their anorectal physiology did not significantly differ from those who had not had a hysterectomy. Again on linear regression analysis of faecal incontinence hysterectomy was not significant. We were not however able to assess from the database whether a vaginal or abdominal hysterectomy may have been significant.

The question remains whether the physiology findings are of any significance. It has been suggested that anorectal physiology is not reliable particularly with respect to non-systematic variations (Ryhammer 1997\(^2\)). It has also been suggested that PNTML bears no relationship to resting or squeeze pressures (Rasmussen 2000). Our finding of insignificant latency differences between the genders and no association between PTNML and squeeze or cough pressures would support this. In an attempt to minimise the non-systematic variations in this study, all physiology was performed by a single operator prior to the inception of the trial. Our physiology results did significantly correlate with the continence scores obtained prior to the physiology assessment. They are also significantly associated with the presenting anorectal symptom. We have shown that within the limitation of anorectal physiology testing there are significant differences in patients dependent upon age, gender, presenting colorectal
symptom, birthing injury and parity. Perhaps of greatest significance, those women with a history of a birthing injury had significantly higher continence scores and poorer physiology results.

Potential Implications

Age and gender are factors beyond medical and political intervention. Birth injury, which has proved to be a significant factor in poorer functional and physiological outcomes is preventable. As given above, between 2495 and 25,537 women in New South Wales in one year sustained potentially avoidable perineal injuries.

Over the past four years several randomised controlled trials have attempted to identify those factors that increase the likelihood of sphincter disruption. Several factors are consistently recognised as correlating with an increased risk. These include first vaginal delivery (Jander 2001, Abramowitz 2000, Mellegren 1999, Donnelley 1998), instrument delivery particularly forceps (Abramowitz, De Leeuw 2001, Eason 2000), median episiotomy (Jander 2001, Zetterstrom 1999, Benifla 2000, Signorello 2000, Eason 2000), augmented labour (Zetterstrom 1999, Samuelson 2000), prolonged second stage (Wood 1998, De Leeuw 2001, De Leeuw 2001²) and a second vaginal delivery after a sphincter injury during a prior delivery (Faltin 2001, Benifla 2000, Donnelly 1998). Factors such as large babies (Handa 2001, Wood 1998, Nielsen 1992), post-term delivery (Zetterstrom 1999), mediolateral episiotomy (Wood 1998, Sultan 1994² Samuelsson 2000, De Leeuw 2001) and gestational age (Jander 2001, DeLeeuw 2001²) have been identified as risk factors in some studies but the findings are not consistent. Following multivariant analysis two factors predominate, firstly primiparous delivery and secondly the use of forceps. The latter of these is potentially avoidable. A further preventative measure, shown to consistently reduce the perineal tear rates by 6%, is perineal massage in the weeks prior to delivery (Eason 2000, Labresque 1999, Shipman 1997). However, in Australia there has been no obvious attempt to reduce the incidence of risk factors known to be associated with perineal injury. Forceps deliveries remain over 10%, labour augmentation remains over 20%, perineal
massage techniques do not appear to be a standard component of antenatal education and a prior sphincter injury or incontinence symptoms do not appear on the inclusion or exclusion criteria for entry to Australian birthing centres. Contrary to this, the Senate Committee has stated that there was no medical justification for caesarian section and that as such it was time for national leadership to reduce the rate of caesarian section. The perineal injury and incontinence rates are possibly the medical justification for caesarian section which the Senate committee failed to identify.

In the UK the female gynaecologists were surveyed as to their birthing choices. Given the scenario of a perfect, uncomplicated delivery 31% still opted for a caesarian section. Of those 80% stated that their choice was secondary to a concern about sphincter injury. Furthermore, introduction of a single risk factor for perineal trauma such as the need for forceps and 68% opted for a caesarian delivery (Al-Mufti 1996). An informed cohort of patients did not choose to put their anal sphincters at risk of damage. A similar study has not been performed in Australia. However, there is an obvious trend among medical professionals or partners thereof to opt for an elective caesarian section over vaginal delivery.

There are also potential legal ramifications in the form of negligence claims for an injury that is potentially preventable. In the UK 60% of patients attending a major centre for anal sphincter repair consequent upon obstetric trauma were seeking legal compensation [personal communication, St Mark’s Hospital, Harrow, UK]. In Australia, 13% of claims closed between 1991 and 2000, as recently reviewed by the Australian United Medical Defence association, involved claims for the consequences of perineal injury during childbirth. Furthermore the number of claims had doubled from the beginning to the end of the review period (Obstetrics Claims Review 2004).

The 1998 Senate Committee report ended with the recommendation that “…the Commonwealth Government work with State Governments to ensure that comprehensive, accurate and current information is made available to all pregnant women on antenatal and birth options.” Given the findings of this and
previous studies and the ongoing implications of perineal birth injury perhaps the time has come for education.
3.2 Long-term follow-up of dynamic graciloplasty for faecal incontinence

Abstract

Objective: This paper presents the long-term functional and quality of life data for patients who have undergone dynamic graciloplasty (DGP) for faecal incontinence.

Methods: All patients (n=38) who had undergone a DGP at this institution between 1993 and 2002 are presented. 33 were available for long-term follow-up (median 60 months) and completed a telephone questionnaire assessing quality of life (QOL), bowel and sexual function and patient satisfaction. All patients had interval anorectal physiology.

Results: At a median follow-up of 5 years 16% of patients reported a faecal continence score <12. Thirty percent of patients had been converted to an end-colostomy. Seventy-four percent reported ongoing morbidity directly attributable to the operation, including a 30% sexual dysfunction rate. Of those patients with a functional DGP 50% reported obstructed defaecation and 64% reported that their bowel dysfunction negatively impacted on their QOL. Age, medical co-morbidity and anal manometry did not correlate with functional outcome. Quality of life scores and patient satisfaction scores positively correlated with continence scores. There was a trend toward higher QOL and satisfaction scores with conversion to colostomy compared with a continence score >12.

Conclusion: The long-term continence rates following a DGP are low with a high peri-operative and long-term morbidity. Selection of those patients who may benefit from DGP in the long-term is yet to be defined.
Introduction

Transposition of the gracilis muscle to reconstruct the anal sphincter was first described in 1952 (Pickrell 1952). The first stimulated dynamic graciloplasty (DGP) procedure was reported in 1991 (Baeten 1991, Williams 1991). Since that time multi-centre trials have attempted to establish the efficacy and place of the procedure. Over the past two years some authors have expressed concern that the outcome may not be as good as previously documented (Baeten 2000). Quality of life assessment has suggested an improvement in the short-term which is not sustained with longer follow-up (Wexner 2002). Failure of peri-operative complication rates to fall with increasing experience has also raised concerns. There are few studies reporting long-term results, with most extending to about two years (Matzel 2001). This paper presents functional and quality of life data with a median follow-up of 60 months.

Methods

Patient Selection

All patients (n=38) who had undergone a stimulated graciloplasty at St George Hospital between October 1993 and March 2003 are presented. The cohort includes patients treated for faecal incontinence resulting from obstetric injury (n=21), direct perineal trauma (n=4), congenital perineal anomalies (n=2), perineal injury from previous anal surgery (n=6) and those patients who underwent neo-sphincter reconstruction after abdominoperineal resection of the rectum for carcinoma (n=5). Those patients with faecal incontinence had pre-operative ultrasound confirmation of a persisting anal sphincter defect despite previous surgery, or evidence of a significant pudendal neuropathy on anorectal physiology. Patients with a rectal carcinoma were selected for DGP reconstruction after curative resection if the rectal tumour was small, moderately to well differentiated on biopsy and macroscopically completely excised.
Operative Technique

Since the results of the first 12 patients from this centre were reported (Kennedy 1996), two major procedural changes have been implemented. Firstly, the gracilis muscle is no longer devascularised as a separate, first-stage procedure. Secondly, the procedure is now performed without a diverting stoma except for those patients undergoing an abdominoperineal resection in which case the stoma is not closed until the completion of neosphincter augmentation and training. In all cases the technique of direct nerve stimulation was used (Williams 1991).

Assessment

All patients completed a pre-operative questionnaire containing an assessment of continence and alteration of lifestyle. Post-operatively, anal manometry was performed at two weekly intervals during the eight weeks of programming. Most patients also underwent manometric assessment twelve months post-operatively and in the last 12 months of follow-up or prior to the formation of a diverting stoma. Anal manometry was performed with a 5 channel, low compliance water perfusion system. Pressures were recorded with the stimulator turned off and with the gracilis maximally stimulated. The voltage required to stimulate the gracilis to a sphincter pressure which was considered sufficient to maintain continence was also recorded.

Long-term assessment included completion of a telephone administered questionnaire containing an assessment of continence using a modified St Mark's continence score (Appendix 1, Vaizey 1997), quality of life (SF-36, Ware 1992), alteration of lifestyle, sexual function and patient satisfaction (Visual analogue scale).

Where available, patient results were compared across time intervals. Group results were also analysed on the basis of functional outcome. The functional categories consisted of a stoma, a functional gracilis with a continence score less than 12 and a functional gracilis with a continence score greater than 12.
Statistical Analysis

Matched parametric data were compared using the t-test. More than two groups were compared using ANOVA, Bonferroni. Where there were less than 20 in each sample size or the data were non-parametric, Kruskall-Wallis was applied. Multivariant analysis was performed with a linear stepwise regression package after transformation of the raw data to a normal distribution (SPSS 11.0).

Results

Thirty-eight patients underwent DGP between 1993 and 2003. The median age at the time of surgery was 62 (18-76). There were 32 females. Thirty-three patients were available for assessment with a median follow-up of 60 months (range1-112months). Three patients have died, one patient is lost to follow-up and one patient has yet to have closure of a pre-existing colostomy for perineal trauma.

Peri-operative morbidity

Data for all 38 patients were available for review. Two patients required revision of the gracilis transposition. One patient with a congenital anorectal malformation had an anomaly of the main vascular pedicle to the gracilis resulting in ischaemia when the muscle was mobilised. In the second patient the gracilis tendon detracted from the ischial tuberosity. Thirteen patients required a total of 18 surgical procedures to replace pacemaker components. Six Nice pacemakers required replacement in under two years due to the short life-span of the battery. Four Nice leads fractured and one lead required replacement as the result of a chronic staphylococcal infection. Six of the Medtronic leads fractured and one Medtronic pacemaker required replacement as the result of fluid leakage into the pacemaker capsule.

Thirteen wounds, five perineal, six thigh and two abdominal developed clinical evidence of local infection. Four required surgical debridement and four required daily dressings for longer than two weeks. Two patients were
documented to have a bullous perineal fungal infection. Wound swabs suggested a Penicillin Sensitive Staphylococcal infection in eight thigh wounds and Streptococcal Faecalis in two perineal wounds. One patient developed a deep venous thrombosis and pulmonary embolus.

In the longer term, the most frequent non-gastrointestinal morbidity reported by 24 patients, involved the donor leg. Eight patients reported pain, seven swelling and eighteen paraesthesia. Of these 16 patients reported that the leg symptoms had a negative impact on their quality of life.

When the first and the last 19 patients were compared, there was no statistical difference in the frequency or type or peri-operative morbidity (p>0.1). The frequency of peri-operative complications did not have an impact on the functional result on multivariant analysis.

Complications following stoma formation have included two parastomal herniae requiring surgical revision. Two patients have also reported an ongoing functional bowel disorder requiring intermittent use of loperamide.

Functional Assessment

At long-term follow-up, 11 patients have been converted to an end colostomy, one patient is awaiting replacement of a fractured pacemaker lead and one patient is awaiting either an appendicostomy for antegrade colonic lavage or an end colostomy for symptoms of obstructed defaecation. The median time to stoma formation was 16 months. A stoma was formed for ongoing faecal incontinence in six cases and for obstructed defaecation for four cases. One patient had an emergency stoma as the result of peritonitis after percutaneous insertion of a caecostomy button for obstructed defaecation.

Of the 22 patients with a functional graciloplasty, the median continence score was 16 (range 2-22, mean 15). Thirteen patients reported daily faecal incontinence. Only two patients were able to defer defaecation for longer than 10 minutes and had any flatus control. Despite the frequency of incontinence
the most commonly reported gastrointestinal complaint was that of obstructed defaecation. Eleven patients (50%) reported evacuation difficulties requiring daily enemas, irrigation or manual assistance to defaecate. An additional five patients reported the need for daily laxatives. Sixty-four percent reported that their current bowel function negatively impacted on their daily activities.

There was no correlation between functional outcome and age, aetiology of incontinence or number of previous perineal procedures.

Quality of Life

Firstly, QOL for the group (n=33) was compared with QOL scores controlled for other patient co-morbidity and for those limitations caused by symptoms from the donor leg. Neither differences were statistically significant (p>0.1, p>0.6 respectively). Quality of life was assessed across three groups of functional outcome; those with a stoma (n=16), those with a functional graciloplasty and a continence score greater than 12 (n=10) and those with a graciloplasty and a continence score less than 12 (n=6). Patients with a functional graciloplasty and a continence score less than 12 had a significantly improved QOL score than either those with a stoma, or those with a continence score greater than 12 (p<0.04). This difference persisted upon re-scoring taking into account other medical co-morbidity including donor leg symptoms. Patients with a stoma did not score significantly different to those patients with a continence score greater than 12(p>0.1). However, there was a trend toward an improved QOL score for those patients with a stoma after controlling for co-morbidity (p=0.06).

Although the total SF36 score was not a statistically significant variant on multivariant analysis of continence, physical limitation scores and poorer mental health scores obtained as individual components of the SF-36 were significant variants (p<0.02 for each).

Sexual Function
Twenty-two patients were not sexually active for reasons unrelated to either the graciloplasty or bowel dysfunction. Only two of the remaining 11 patients reported having sexual activity. Both of these patients reported dyspareunia that developed after the procedure. A further six patients reported that from the time of the graciloplasty sexual relations had become too painful. Three patients reported their ongoing incontinence as the reason for abstaining from sexual activity.

**Manometry**

The pressures generated by the DGP with the stimulator off, maximally stimulated and stimulated to a functional level did not vary significantly over time (p>1.0, p>0.3, p>0.5 respectively) [Fig 1].

![Manometry Graph](image)

**Fig 1: Dynamic Graciloplasty pressures generated with maximum stimulation, with functional stimulation and with the stimulator off over time. First stimulation taken at one month, n=35 patients; 12 months, n=23 patients; last stimulation taken at a median of 60 months, n=29 patients.**

There was a significant increase in the voltage required to achieve the functional resting pressure over time (p<0.009) [Fig 2].
Fig 2: Voltage required to generate functional dynamic graciloplasty pressures over time

There were no significant pressure differences, nor voltage requirement differences across the functional groups (p>0.5).

Patient Satisfaction

Sixty percent of patients rated their satisfaction with DGP as 50% or better on a visual analogue scale. This correlated strongly with the continence score at the time of the assessment (p<0.001) [Fig 3].

Fig 3: Patient procedural satisfaction scores compared across functional outcome groups. Patients with a stoma, n=11; Patients with a continence score >12, n=16; Patients with a continence score <12, n=6.
However, patients with a stoma at long-term assessment were statistically more likely to report that their function was better following the formation of the stoma than during the period of functional incontinence (p<0.001). Similarly, patients with a functional graciloplasty and a continence score greater than 12 were more likely to report that their function was worse than prior to the graciloplasty (p<0.001).

Discussion

Peri-operative morbidity and function

DGP is recognised as a procedure with a high morbidity, with an average of one complication factor reported per patient (Chapman 2002). Similar to Baeten et al (Baeten 2000), our data suggest that the expected rate is two complications per patient. Comparison of the first and last 19 patients confirmed the findings of similar studies that the number of procedures previously performed by a particular surgeon does not impact on the functional outcome and does not affect the number or type of complications (Matzel 2001). Given that this procedure is usually performed in specialised units it is likely that the documented failure rates of 40-60% (Wexner 2002, Mander 1999) are a reflection of non-controllable factors, at least at the present time.

This review highlighted three post-operative complications. Pain, swelling and paraesthesia in the donor leg have been documented in up to 30% of patients (Baeten 2000). Although we have reported a total incidence of 73% only one third of these patients reported that their leg symptoms negatively impacted on their quality of life. Furthermore, quality of life scores were not statistically different when the leg symptoms were taken into account. It remains unclear whether the pain is referred from the stimulated gracilis muscle or the result of local trauma. The swelling and paraesthesia are likely to be due to the latter although the symptoms are often disproportionate to that expected from the extent of the dissection. There were no saphenous nerve injuries recognised intra-operatively in this study and no recognised injuries to the main trunk of the long saphenous vein and yet 24 patients reported symptoms which could be
directly related to injury to either of these structures. It is possible to understand nerve injury when a preceding first stage devascularisation procedure had been performed and perhaps in a one-stage procedure, even when the nerve had been easily identified, as a result of a traction injury.

Obstructed defaecation is reported to be a significant problem in 23-90% (Baeten 2000, Rosen 2002) of patients and in our study was responsible for half of the conversions to colostomy. Previous studies have suggested that obstructed defaecation may precede the DGP (Mander 1999). The problem is likely to be multi-factorial, and the physiology is poorly understood. A pre-existing neurogenic dysfunction could prevent evacuation if the patients were to have a functioning anal sphincter. Two observations support this theory. Firstly patients who have undergone an abdominoperineal excision and graciloplasty have very high rates of obstructed defaecation (Christiansen 1998). The neo-rectum of these patients is devoid of the normal neural supply and has been documented to have reduced sensitivity. Secondly, a lower pre-operative rectal sensitivity has been shown to correlate with a poorer functional outcome following DGP (Korgsen 1995, Sielezneff 1999). A pre-operative defaecating proctogram in DGP patients is unreliable because of their inability to hold rectal contrast (Mander 1999). Rectal sensitivity may therefore be a useful pre-operative investigation to indicate those who are likely to develop symptoms of obstructed defaecation. Consideration could then be given for placement of an antegrade colonic lavage device simultaneously or early in the post-operative period. Conversion to a stoma was avoided in two study patients by an aggressive policy of antegrade colonic irrigation.

Very few studies have assessed post-operative sexual function. Wexner recorded a 25% incidence of sexual dysfunction but the type of dysfunction and its relationship to either the preceding faecal incontinence or the graciloplasty surgery were not given (Wexner 2002). The age group of the patients considered for a DGP increases the likelihood of sexual abstinence. Nine of our cohort had been widowed prior to the DGP and had not considered repartnering irrespective of their continence. Furthermore, many patients will have had preceding perineal surgery which may impact on sexual function, particularly in
causing dyspareunia. Our data suggest that the DGP results in new symptoms of sexual dysfunctional in 27%. However, prospective assessment of sexual function requires further investigation.

**Manometry**

There was no correlation between the manometric function of the muscle and patient continence at the completion of augmentation or in the months to years following, consistent with several earlier studies (Baeten 2000, Wexner 2002). The increased voltage requirement over time has also been reported previously (Mander 1999). It has been suggested that fibrosis around the lead electrode may be responsible for the increased voltage required but this is speculative. The impact on faecal continence of increasing the voltage in order to increase the manometric reading has not yet been assessed. However, in this study, the voltage was only increased if the patient was experiencing episodes of faecal incontinence. Data on the objective response to the voltage increase were not available.

**Quality of Life and Patient Satisfaction**

Wexner et al recently reported a significant improvement in quality of life score in the first twelve months post-operatively and a positive correlation with functional outcome (Wexner 2002). The data presented in this study is the first to report a long-term quality of life assessment. Functional outcome continues to correlate with quality of life scores. However, contrary to patient reports that they are functionally much better with a stoma than a poorly functioning DGP, there was no statistical difference in the quality of life scores of those with a stoma and those with a continence score greater than 12. There is a trend toward a statistical difference when medical co-morbidities such as back pain, ischaemic heart disease and cerebrovascular disease are taken into account. The sample size of each subgroup may have resulted in a type II error. However, Wexner's results suggested there that general health did not impact on functional performance (Wexner 2002).
Multivariant analysis demonstrated a significant correlation between continence scores and patient mental health and physical limitations. The physical limitation factor is not surprising given that physically mobile patients are likely to experience fewer time dependent incontinence problems. However, the mental health association may be either the cause or consequence of the documented continence problems.

Visual analogue or subjective patient satisfaction scores are often inconsistent with the objective functional outcome for an individual patient. Consistent with previous reports (Christiansen 1998), overall patient satisfaction is significantly greater the lower the continence score (p<0.001). However, stoma patients report greater satisfaction than patients with incontinence (p<0.01), despite there being no significant difference in quality of life scores.

Several patients reported that the experience of going through the DGP prepared them mentally and emotionally to accept the need for a colostomy. Whether that peace of mind warrants the financial burden and co-morbidity of the procedure remains questionable. One recent cost analysis has suggested that there are still insufficient data to compare a life-time stoma with a graciloplasty for all patients (Chapman 2002). There is little doubt that a DGP which results in a continent patient is cost-effective (Adang 1998) and positively impacts on patient quality of life in the short-term (Mander 1999). However with only 16% of patients maintaining a continence score of 12 or less at five years and the absence of clearly identified prognostic factors, the debate may revolve around the financial and social costs of a stoma compared with a poorly functional DGP. One study compared social role function and quality of life scores between patients undergoing an ultra-low anterior resection and re-anastomosis and those with a colostomy (Graumann 2001). The ultra-low resection cohort had similar bowel functional complaints to the post-operative DGP patient. Social role function was significantly reduced in those with the low anastomosis and quality of life scores showed a trend toward improvement in those patients with a stoma. Quality of life scores in this study also suggest a trend toward an improvement with stoma formation. Furthermore, patients
perceive that their function post-stoma formation is improved. However, the statistical validity of these trends remain to be tested.

Conclusion

Dynamic graciloplasty significantly improves patient quality of life and anal continence for some patients. However, despite increased experience, morbidity remains high and the long-term outcome for the majority is poor. Significant prognostic factors remain to be identified. The mechanism of both continence failure and surgical morbidity remains poorly defined in many patients and requires further investigation. Presently, the individual patient can expect a 16% chance of faecal continence at 5 years with at least one surgical or functional morbidity as a result of the surgical intervention.
3.3 Re-do anal sphincter repair

Abstract

**Background and aims:** The small number of studies on the long-term results of surgery for faecal incontinence have sometimes shown disappointing results. This is the first report on the long-term results of re-do overlapping anal sphincter repair.

**Patients and methods:** The results of repeat anal sphincter repair on 23 patients were previously reported at a median follow up of 20 months. Thirteen patients (65%) had felt that they were 50% or more improved pre vs. post op. These patients were reassessed at a median of 5 years (range 48-86 months) using a questionnaire and telephone interview to determine current bowel function, continence, and restriction in activities of daily life and overall satisfaction with the results of surgery.

**Results:** Twenty-one patients, median age 47 years (range 27-66 years) were contacted. One patient was lost to follow up and one had died of pancreatic cancer. Thirteen patients (60%) reported symptom improvement of 50% or greater. Two patients were fully continent, 8 had experienced no urge incontinence in the past four weeks and 12 reported no passive leakage in the past four weeks. Eleven patients reported some control of flatus.

**Conclusion:** Clinical outcome indicates that the long-term results of redo anterior sphincter repair show a sustained improvement in continence.
Introduction

Although anterior overlapping sphincter repair has been shown to produce a good short-term clinical result in up to 80% of patients (Engel 1994, Young 1998, Briel 1998, Malouf 2000), a study of long-term functional outcome has suggested that function deteriorates over time (Pinedo 1999). Similarly, the results of post-anal repair have been disappointing in the longer-term (Engel 1994, Setti-Carraro 1994).

The surgical options available to those who fail a simple repair are either a permanent colostomy (Porter 1989) or one of the newer operations such as dynamic graciloplasty (Baeten 1991, Wexner 1996), or artificial bowel sphincter (Lehur 1996, Wong 1996, Christiansen 1989). These neosphincters have high complication and revision rates and are, in addition, quite costly.

In patients with a persistent sphincter defect but an intrinsically functional external sphincter a repeat repair would appear to have the advantages of being less complex and less expensive and of being associated with lower complication and revision rates. The short-term follow-up of such patients who had undergone a redo anal sphincter repair demonstrated a significant improvement in continence scores and ability to defer defecation (Pinedo 1999).

This study is the first to report the long-term outcome of repeat overlap repair in patients who have failed one or more previous repairs.

Patients and Methods

Twenty-three patients median age 47 years (range 27 to 66 years) underwent repeat repair of an anterior obstetric-related sphincter injury in the three-year period from May 1994 to May 1997. This group represents about 10% of all sphincter repairs carried out at our hospital during this period.
Twenty one were available for follow up. In ten this was made by postal questionnaire and in eleven by telephone interview. Details of the original 23 patients, including surgical and obstetric history have been previously been described (Pinedo1999). All had been selected after failure of a previous anterior anal sphincter repair or repairs, on the basis of a residual external sphincter defect confirmed on endoanal ultrasound but a clinically functional muscle.

In the twenty-one patients available for follow-up, excluding attempted repair at the time of obstetric trauma, 13 patients had undergone one previous surgical repair and eight had undergone two previous surgical repairs. Four patients had undergone a previous repair at our hospital, 16 by colorectal surgeons at other hospitals and three by gynaecologists.

**Assessment**

Patients were assessed by a postal questionnaire or by telephone interview if the questionnaires were not returned. The results were assessed by an independent clinician outside the surgical team, who had not been involved with the initial post-operative assessments. Questionnaires assessed current clinical status, quality of life and Wexner continence grading scale [Jorge 1993, appendix 2]. The same information for each patient was available from the earlier post-operative study (median 20 months) for comparison.

**Statistical analysis**

Statistical analysis on the median values before and after surgery was performed using the Wilcoxon matched pairs signed rank tests. The Speakman’s rank correlation test was used to relate the changes in variables to the patients’ assessment of percentage improvement and satisfaction.
Results

Of the 23 consecutive patients undergoing re-do anterior anal sphincter repair, one patient had died of an unrelated malignancy and one could not be contacted. Twenty-one patients (91%) were therefore available for long-term assessment.

The median time from sphincter repair to this assessment was 60 months (range 48-86). Two patients (9%) had required further surgery for faecal incontinence. One patient had a colostomy without further surgery to the pelvic floor, the other underwent a post-anal repair with a resulting further deterioration in symptoms. Nineteen patients were available for long-term functional assessment of the sphincter repair. No patients had had any further pregnancies.

As previously reported there was again no relationship found between patient age, number of previous repairs or the use of a covering colostomy and clinical outcome after the repeat repair.

Assessment:

Of the twenty-one patients contacted four patients (19%) reported a overall deterioration in symptoms. A further two patients reported that the re-do repair had made no difference to their incontinence. One patient had undergone a permanent colostomy and three patients are awaiting formation of a permanent colostomy. On the satisfaction scale of 0-10 (very dissatisfied to completely satisfied) the median score was seven with a range from zero to ten. Nine patients (43%) rated their satisfaction with the results of the operation as 9 or 10. Similar results were found at a median follow-up of 20 months, with these twenty-one patients reporting a median satisfaction of seven, range zero to ten and six patients (29%) rating their satisfaction as nine or ten. [Figure 1]
Of the 19 patients available for functional assessment, two patients were fully continent, 8 had experienced no urge incontinence in the past 4 weeks and 12 reported no passive leakage in the past 4 weeks. Eleven patients reported some control of flatus.

For 12 patients (63%) symptom improvement was reported to be 50% or greater at the 60 month follow-up compared to 14 patients (74%) at the 20 month follow-up. The median reported symptom improvement remained constant at 60% [Figure 2].

At the 60 month follow-up 13 patients (68%) rated their bowel control greater or equal to 7 on a scale of 0 to 10 (no control to perfect control). This data was not available from the 20 month follow-up for comparison.
Median Wexner continence grading scores improved from a median score of seven (range 1-20) at the 20-month assessment to six (range 2-19) at the 60-month assessment [Figure 3].

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Figure 3: Wexner continence scores pre-operative, 20 month and 60 month following re-do anal sphincter repair. (median in bold type)

The ability to defer defaecation however deteriorated with a median of 10 minutes reported at the 20-month assessment to a median of four minutes at the 60-month assessment. However, of the 13 patients unable to defer defecation for less than five minutes, nine reported that their stool was usually soft to liquid. Only two however reported the use of regular loperamide and only two have been referred for biofeedback retraining so far.

Seven patients now reported difficulties with defecation. Two patients reported that evacuation was incomplete. Six reported the need to strain. Two of these patients were taking regular loperamide. Only one patient however reported the use of enemas or laxatives and this was on a monthly basis only.

Lifestyle restrictions secondary to the incontinence were reported to have occurred less than once a month in 11 patients. Of the eight patients who reported lifestyle restrictions greater than monthly, seven specifically commented that their ability to exercise or to join sporting activities was restricted. Only two patients reported restrictions on a daily basis.
Of the seven patients who had failed a re-do sphincter repair rating their bowel control as less than five, six had reported repair failure with incontinence to solid and liquid faeces and flatus at less then six months. One patient who reported a decline in function at 73 months is currently under investigation for a recto-vaginal fistula.

There was a significant correlation between the improvement in the Wexner incontinence scores and the improvement in ability to defer defaecation and the patient’s assessment of improvement and satisfaction (p<0.001).

Discussion

The long-term results of redo overlapping anterior sphincter repair appear to show persistent benefit from the repair.

Assessment of outcome after surgery for faecal incontinence has, in the past, been confined to a simple satisfaction scale with perhaps the addition of a limited continence grading scale. Patients in this trial were assessed with validated scoring systems (Vaizey 1997). The accuracy of the results obtained by telephone however is unknown. Although several studies have used telephone questionnaires to assess faecal and sexual function (Malouf 2000, Sheu 2003), there are no published attempts to compare the results with a postal interview or face to face interview.

The five year outcome following surgery for faecal incontinence is now known for anterior sphincter repair and post anal repair; failure after each is common with the former achieving acceptable results in 60-70% of patients and the latter approximately 30% (Jameson 1994, Setti-Carraro 1994). Dynamic graciloplasty, followed for the same period has achieved similar results as the anterior sphincter repair but with a much greater reported morbidity and cost (Baig 2000, Niriella 2000). Furthermore, the expected lifespan of the graciloplasty stimulator is approximately seven years (Baeten 1995). The outcome of sufficient numbers of patients over a similar period of follow up is
not yet known for artificial bowel sphincter. The artificial bowel sphincter is easy to implant but removal owing to pressure necrosis or infection has been necessary in over 15% of patients (Mander 1999). Given these data, there is general agreement that neither procedure should be advised where it is felt that a sphincter repair has a reasonable prospect of success. However if the patient has already had a failed repair the clinician may feel reluctant to advise a second, preferring to proceed directly to an artificial sphincter or dynamic graciloplasty. The results of this study continue to demonstrate a high rate of patient satisfaction (60%) with the outcome of re-do anterior sphincter repair at a median follow-up of 60 months. This rate is similar to the best results that have hitherto been reported for the alternative procedures. Furthermore, Wexner continence scores continued to improve throughout the follow-up period. Good correlation was found between the percent improvement and satisfaction scores, and the ability to defer and Wexner scores.

Case selection is important with this small group of patients being about 10% of all sphincter repairs carried out at our Hospital. All patients in the study had a persisting anterior sphincter defect on anal ultrasound but in addition they were all deemed to have reasonable functioning external sphincter muscle as judged by clinical assessment including inspection and palpation of the muscle contraction.

The optimum treatment for patients with a poor functional result and persisting external sphincter defect is yet to be defined. Long-term assessment of all forms of repair is limited. However, up to 50% of patients who undergo primary anterior sphincter repair will not have a successful outcome (defined as no further surgery and urge incontinence monthly or less)(Malouf 2000). Re-do anterior sphincter repair is one option for these patients which carries minimal cost and morbidity. The short-term follow-up of functional outcome proved this procedure to be as efficacious as graciloplasty and artificial anal sphincter (Pinedo 1999). Long-term follow-up (median 60 months) has shown sustained efficacy. Those patients who failed outright did so in the first six months. Improvement in Wexner incontinence scores and patient satisfaction scores remain unchanged. The reported decline in function in the three continent
patients is concerning. However, at a median follow-up of 60 months the outcome suggests that repeat repair should be considered before more involved procedures in cases with a defective but intrinsically functioning external sphincter.
3.4 Extracorporeal magnetic stimulation of the pelvic floor; impact on anorectal function and physiology. A pilot study

Abstract

Aim: To investigate the effect of extracorporeal magnetic stimulation on anorectal function and physiology

Methods: A pilot study comparing the physiology of 10 incontinent (9F:1M) and 5 (4F:1M) continent patients with and without perineal magnetic stimulation (10Hz and 50Hz) was performed. The 10 incontinent patients were then treated with two sessions weekly for five weeks of perineal magnetic stimulation. At treatment completion, pre and post continent scores and resting and squeeze anal pressure were compared. Patients also reported symptom improvement and satisfaction on a linear analogue scale.

Results: The mean age was 57. Sitting resting and squeeze anal pressures were significantly greater than lying pressures (p=0.007, 0.047). Both 10 and 50Hz stimulation effected a significant increase in anal pressures compared to the baseline resting pressure (p=0.005). The baseline squeeze pressures however were higher than the stimulated pressures, significantly so compared to 50Hz pressures (p=0.022). Following six weeks’ treatment there was a statistically significant increase in resting and squeeze anal pressures and a significant decrease in continence scores (p=0.007, p=0.008, p=0.017). The mean percentage subjective improvement was 16 percent and the mean patient satisfaction score was 3.3, positively correlating with an improvement in the continence score.

Conclusion: Extracorporeal magnetic stimulation results in a significant increase in resting anal pressure irrespective of pre-treatment continence. Although the subjective improvement in continence following treatment is small, there is a significant improvement in both resting pressures and patient continence scores.
Introduction

Faecal incontinence affects between 7 and 15% of the general population (Soffer 2000, Lam 1999). Current therapies provide symptomatic improvement in up to 70% of patients but the treatments are often invasive and the physiological effects are inconsistent (Rosen 2001, Norton 2001). Magnetic stimulation induces an electrical field sufficient to produce neural membrane polarisation. From urological studies this membrane polarisation stimulates efferent pudendal nerve activity resulting in increased urethral closing pressures and reduced detrusor instability (Yamanishi 2000, Fujishiro 2000). Thus far the effect of magnetic stimulation on anorectal function has only been assessed with sacral nerve electromagnetic stimulation which requires radiological positioning and is limited by patient body mass (Morren 2001). Unfortunately the results have been inconsistent (Shafik 2000).

Extracorporeal magnetic innervation (ExMI) is a non-invasive means of delivering magnetic stimulation without xray exposure. Using this technology we have reassessed the effect of pelvic floor magnetic stimulation on anorectal function and symptoms of faecal incontinence.

Patients and Methods

Ten patients (9 female), mean age 62, were recruited from patients referred for anorectal physiology to investigate symptoms of faecal incontinence. Inclusion required a history of one or more episodes per month of incontinence to solid faeces. Patients were also required to have an intact internal anal sphincter on endo-anal ultrasound. Five patients (4 female), mean age 48 with normal continence were recruited as controls. Exclusion criteria for both groups included any implantable devices, recent surgery, pregnancy and any history of cardiac arrhythmia.

A complete obstetric and surgical history was obtained from all patients and a Wexner continence score completed. Anorectal manometry was performed with a stationary, six radial channel, water perfusion catheter with computer acquisition and analysis of data (Neomedix, Sydney, Australia). The cranial
distance between the six manometry channels was 0.75cm, such that the pressure was measured from 0.75cm to 3.75cm from the anal verge. The sixth channel measured rectal pressure. The normal ranges for resting and squeeze pressure with the patient lying in the left lateral position in our laboratory are 60-100cmH$_2$O.

Patients were initially asked to lie in the left lateral position. An anorectal manometry catheter was then inserted and the position in the anal canal confirmed manometrically. In particular, the first channel was required to be in the anal canal as evidenced by a resting pressure greater than zero. All treatment patients then underwent formal manometric assessment of resting and squeeze pressures. The catheter was then taped to the buttock and the patient carefully positioned on the Chair (Neocontrol®, Neotonus, Marietta, GA, USA). The position of the catheter within the anal canal was again confirmed manometrically. A baseline resting and squeeze pressure in the sitting position was recorded for all patients.

**Technique of Extracorporeal Magnetic Stimulation**

The patient was asked to sit upright in the Chair with both feet on the floor. The electromagnetic pulse is generated in the external unit and then transmitted to the base-plate in the seat. The generator creates pulses of 275μs. The frequency was commenced at 10Hz and the amplitude is slowly increased until the patient is aware of the stimulation. The patient is then asked to adjust the position of their perineal area over the stimulating focus. The strength of the stimulation is slowly increased toward 100% of the maximum. Patients report their maximum tolerated level of stimulation and the treatment is applied at this setting. Stimulation at a frequency of 10 Hz is applied for five seconds followed by five seconds rest for a total of 10 minutes. Patients were then given a two minute rest period during which resting anal pressure and a voluntary squeeze pressure is recorded. A second 10 minute period then proceeds with 50 Hz administered, again in five second on/off cycles. At the completion of this a
further two minutes is allowed to elapse before taking a final resting and squeeze anal pressure measurement.
The treatment cohort then underwent a five week course of twice weekly, 20minute sessions. Stimulation was provided at dual frequencies as above, at the maximum tolerated stimulation. During the treatment sessions continuous anorectal monitoring was not performed. At the completion of treatment patients underwent repeat anorectal physiology, completed another Wexner continence score and a linear analogue bowel function improvement and patient satisfaction score. The linear analogue scores required the patient to rate subjective symptom improvement and their satisfaction with the change from zero, being no improvement and completely dissatisfied, to ten, being symptom resolution and complete satisfaction. From the bowel diaries an accurate Wexner continence score was calculated.

All protocols were approved by South Eastern Area Health Service Ethics Committee.

Statistical Analysis

Nominal data was assessed with a chi-squared test. Paired non-parametric scaled data was assessed with the signed Wilcoxon log rank sum test. Unpaired data was analysed using the Mann-Whitney test. A p value of 0.05 (two-tailed) was considered significant.

Results

Patients were matched across the groups for age, parity, obstetric injury and previous perineal surgery. In the treatment group five patients had either a tear or an episiotomy and four patients had undergone previous anal surgery, two haemorrhoidectomies and two internal sphincterotomies. All patients had intact anal sphincters on endoanal ultrasound. Significantly more patients in the treatment group had undergone a hysterectomy and reported symptoms of urinary incontinence. (Table 1) The mean baseline continence score in the treatment group was 14. These continence scores did not correlate with baseline lying or sitting resting or squeeze pressures.
There was a significant increase in both the maximum resting and squeeze pressures when the patient was seated on the chair compared to lying pressures. The resting pressure increased by a mean of 59 cmH$_2$O and the squeeze by a mean of 57 cmH$_2$O (p=0.007, p=0.047 respectively).

The resting and squeeze pressures in the following paragraphs are all sitting pressures. Quantitative values are given in Tables 1 and 2.

In both the treatment and control groups baseline squeeze pressures were significantly greater than the baseline resting pressures (p=0.005, p=0.043 respectively). Comparing the treatment and control groups, the treatment group baseline resting and squeeze pressures were significantly lower than the control group pressures (p=0.04, p=0.014 respectively). The treatment group
continence scores were also significantly greater than those of the control group (p=0.002).

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Table 2: Treatment group pressures (cmH\(_2\)O), pre and post treatment incontinence scores (ICS), % improvement scores and satisfaction scores (SAT). [MRAP=maximum resting anal pressure, Sq= squeeze]

All patients tolerated the treatment without reported discomfort at a maximum stimulation over 80 percent.

Applying 10Hz magnetic stimulation resulted in a significant increase in the anal pressure in the treatment group when compared to the baseline resting pressure (p=0.005). The mean increase was 32 cmH\(_2\)O (median 42 cmH\(_2\)O). Only one patient had a pressure increase of less than 10 cmH\(_2\)O. In three patients the increase was greater than the baseline squeeze pressure. However, in the other seven patients the baseline squeeze pressure was higher.
than the pressure generated with 10Hz stimulation but the difference was not significant (p=0.103). (Figure 1)

![Graph showing anal pressures](image)

**Figure 1:** Individual patient resting, squeeze, 10Hz and 50 Hz anal pressures (cmH$_2$O). Patients 1-10 are treatment patients. Patients 11-15 are controls.

In the control group, 10Hz stimulation raised anal pressures in all patients. The mean pressure increase was 36 cmH$_2$O (median 55 cmH$_2$O), which was statistically significant (p=0.043). The pressure increase with 10Hz stimulation was significantly less than the increase with a voluntary squeeze (p=0.043).

Applying 50Hz magnetic stimulation resulted in a significant increase in the anal pressure in all patients in the treatment group when compared to the baseline resting pressure (p=0.005). The mean increase was 21 cmH$_2$O (median 27 cmH$_2$O). The pressure increases however were significantly less than those generated by the patient during a voluntary anal squeeze (p=0.022). Furthermore the mean increase in pressure was significantly less with 50Hz stimulation than 10 Hz (0.023).

In the control group, 50Hz significantly raised anal pressure by a mean of 21 cmH$_2$O (median 34 cmH$_2$O) compared to the resting pressure (p=0.042). The resultant pressure was again significantly less than baseline squeeze pressure (p=0.043).
The anal pressures measured in the treatment group with 10 and 50Hz stimulation were greater than the pressures measured in the control group, although the differences were not statistically significant (p=0.06). Given the higher baseline measurements in the control group however, the absolute increase was significantly greater in the treatment group (p=0.03).

In all control patients the voluntary squeeze pressures were greater than the pressures generated by 10Hz stimulation and the 10Hz pressures were greater than the pressures generated with 50Hz stimulation.

In the treatment group seven patients generated voluntary squeeze pressures that were higher than the 10Hz pressure and eight generated pressures greater than the 50Hz pressure. Furthermore in nine of the ten treatment patients the pressures generated with the 10Hz stimulation were greater than the pressures generated with 50Hz stimulation.

At the completion of six weeks treatment there was a significant decrease in the continence scores from 14 to 12 (p=0.017). There was also a significant increase in the lying MRAP (p=0.007). The mean increase was 21 cmH₂O which is a 37 percent increase from the baseline resting pressure. There was also a significant increase in the voluntary lying squeeze pressure with a mean increase of 32cmH₂O or 23% from baseline (p=0.008). The mean subjective improvement reported was 16 percent (0-50%). The mean patient satisfaction score was 3.3 (0-8). Both of these subjective scores positively correlated with the post-treatment incontinence score (p=0.048, p=0.01 respectively) but not the anal resting or squeeze pressures (p>0.89).

**Discussion**

Extracorporeal magnetic stimulation applied via a chair apparatus has been reported to improve objective and subjective measures of urinary incontinence (Chandi 2004, O’Sullivan 2003, O’Sullivan 2003²). Prior to this study the effects of extracorporeal perineal magnetic stimulation on faecal continence and anorectal manometry had not been described.
Non-invasive sacral magnetic stimulation has been shown to activate large sacral nerve fibres, which via the pudendal nerves, innervate the striated sphincters and pelvic floor muscles (Jost\textsuperscript{2} 1994). Morren et al demonstrated a median increase of 12 mmHg in resting anal pressure with 5Hz sacral nerve magnetic stimulation (Morren 2001). However, there are likely to be significant differences in the stimulation provided by a perineal electrode compared to a sacral electrode. Firstly, perineal stimulation would be unlikely to penetrate to the sacral nerve roots hypothesised to augment pelvic floor contraction. Conversely, perineal stimulation may be more likely to circumvent the problem of proximal pudendal neuropathy, which resulted in Morren failing to stimulate a response in 25 percent of faecal incontinence patients. Secondly, Fall suggested that the equivalent of 50-100 Hz electrical sacral stimulation would be required to stimulate the pudendal nerves (Fall 1984), much greater than the frequency required to generate a contraction if supplied via the perineum. Finally pudendal nerve stimulation alone does not explain the manometric changes seen in this study over time.

The pudendal nerve supplies the striated pelvic floor muscles including the external anal sphincter. However, these muscles are responsible for less than 10\% of the resting anal pressure (Swash 1985) which we have shown significantly increase over time. It is possible that perineal stimulation results in polarisation of the peripheral small fibres of the pelvic floor generating an action potential both in the pudendal nerves, as evidenced by the immediate increase in anal pressure, and the sympathetic nerves, as evidenced by the increase in resting pressure over time. During pelvic EMG, a sustained increase in tonic activity of the sphincteric motor unit has been documented (Fall 1984). However, whether this effect is due to modification of synapses, a local change of amount of signal or to re-routing of pathway systems within the central nervous system is speculative. The neurophysiology of perineal magnetic stimulation is less clear. We chose to investigate the effects of 10Hz and 50 Hz based on the urological data suggesting that 10Hz was required to inhibit detrusor instability and therefore possibly rectal hypersensitivity and at least 20 Hz for external urethral meatus contraction and therefore anal sphincter
contraction (Yamanishi 2000). Further investigation is required however our results would suggest that 10Hz effects the greatest response on the anal sphincter complex. It may have been however that anal sphincter fatigue resulted in a reduction in the response seen with 50Hz stimulation. Against this however, the final 10Hz trace for each patient resulted in higher pressures than the first 50Hz trace even though there was a two minute rest period between the two stimulation periods. The same decrease was not seen with the subsequent 50Hz stimulations.

The mean pressures generated were no greater than the patient’s squeeze pressure for either ten or 50Hz stimulation in the control group. However in the treatment group, six patients had anal pressures generated that were greater than their squeeze pressures. There were no factors specific to these patients to explain the different response. Furthermore, the Chair was able to induce squeeze pressures in the treatment group that were not significantly different from those of the control group, even though the baseline squeeze pressures were significantly different for the two groups. The sphincter complex in incontinent patients was capable of contracting as strongly as the patients with normal continence. If pelvic floor exercises are able to improve anal pressures and anal continence (Norton 2003), our results would suggest that the chair may result in a further improvement as evidenced by the decrease in continence scores post-treatment.

Extracorporeal magnetic stimulation is non-invasive and is tolerated well by patients. The major limiting factor is cost. The chair apparatus alone costs $40,000AUS and a complete course of treatment costs $80AUS. Furthermore there is no data on the long-term effect of the treatment for either urinary or faecal incontinence. However, our results would suggest that although patient perceived improvement following six weeks of treatment is small, there is a statistically significant increase in resting anal pressure and a statistically significant reduction in baseline continence scores.

**Conclusion**
Extracorporeal magnetic stimulation results in a significant increase in resting anal pressure irrespective of pre-treatment continence. Although the subjective improvement in continence following treatment is small, there is a significant improvement in both resting pressures and patient continence.
3.5 Long-term indwelling seton for complex anal fistulae in Crohn’s disease

Abstract

**Background:** To review the results of long-term indwelling seton or depezzar catheter in the management of perianal Crohn’s disease.

**Methods:** A retrospective case review from data extracted from a prospective endorectal ultrasound database was performed. All patients underwent an intra-operative endorectal ultrasound to identify the extent of the fistulae and to assess anal wall thickness. Fistulae were classified by Parks’ criteria. All patients then underwent insertion of a seton or depezzar catheter under ultrasound guidance. All patients were followed clinically and with endorectal ultrasound by the senior author. Outcome measures included symptom control, number of procedures required, faecal continence and reduction in anal wall thickness.

**Results:** Twenty-eight patients with 43 complex perianal Crohn’s fistulae were identified. Median follow-up was 13 months (range 2 - 81 months). Six patients (21%) developed recurrent or new perianal symptoms while the seton was insitu. Three patients (11%) required further surgical intervention. The median anal wall thickness at the time of diagnosis was 18.5mm reducing to a median of 14mm following seton insertion and symptom control \((P < 0.02)\). No patient reported deterioration in faecal continence following seton insertion. In multivariate analysis patient age \((P < 0.005)\), reduction in anal wall thickness following seton insertion \((P < 0.04)\) and longer follow-up \((P < 0.03)\) were significant predictors of long term symptom control.

**Conclusion**
Long-term indwelling seton is an effective management modality for complex perianal Crohn’s fistulae which does not negatively impact on faecal continence. Clinical symptoms and course are associated with anal wall thickness as measured by endorectal ultrasound.
Introduction

Perianal fistulae occur in up to 30 percent of patients with Crohn's disease (Schwartz 2002). They are often recurrent, complex and associated with ongoing perianal sepsis (Makowiec 1997). The literature presents opposing views on the role of surgery in the treatment of this difficult condition. Fistulotomy is argued to be safe in superficial fistulae however incontinence rates of up to 50 percent are reported (Allan 1988). There has also been concern expressed that fistulotomy may aggravate anal lesions, which in up to 40 percent of patients, fail to heal (Hellers 1980). More-over many perianal Crohn's fistulae are high, complex fistulae. An alternative method of symptom control is long-term indwelling seton or mushroom catheter drainage. This method has previously been reported to be effective for symptom palliation over a follow-up period of two to 84 months (White 1990). We present our series of 28 patients with complex perianal Crohn's fistulae managed by one surgeon with a long-term indwelling seton or mushroom catheter.

Methods

A retrospective case review from data extracted from a prospective endorectal ultrasound database of all patients with perianal Crohn's fistulae treated by the senior author with a long-term indwelling seton or mushroom catheter. Patients were referred after exhaustion of the medical options by gastroenterologists with a particular interest in Crohn's disease.

All patients had pathological confirmation of Crohn's disease. All patients underwent a pre-operative transanal ultrasound to delineate and define the extent of the fistula and abscess cavities and to assess anal wall thickness (AWT) as a marker of activity of perianal Crohn's (Solomon 1995, Solomon 1996). A 7-10mHz radial transducer with a balloon filled with degassed water for the rectum and a rigid cone for the anal canal was used (Brüel & Kjaer, Naerum, Denmark, 1850). Serial scans were performed from the mid-rectum to the dentate line.
Classification of the fistulae was according to the criteria established by Parks et al (Parks 1976).

All setons and mushroom catheters were inserted under general anesthesia and with intraoperative transrectal ultrasound guidance. Patients are placed in the lithotomy position. A probe is passed along the fistula tract usually from the external to the internal opening. A silk or nylon suture is passed along the gutter of the fistulotomy probes through the fistula tract. A silicon seton is then tied to the suture and pulled through the tract. This is secured loosely in a loop with the knot ends usually left internally in the cavity. Skin or tags are divided only if long-term cosmesis and quality of life will be expected to improve.

Patients were reviewed in the senior author's rooms and underwent interval transanal ultrasound. Outcome measures included symptom palliation, continence, AWT and recurrent sepsis. Symptom control and faecal continence was determined by a clinician initiated qualitative assessment. Symptom control was defined as minimal perianal discharge and the absence of perianal pain. Faecal continence was defined as passive and urge continence for both flatus and faeces.

Statistical Analysis

Pre and post-treatment AWT were assessed with the paired Student t-test. A P value < 0.05 was considered significant. Univariate and multivariate analysis was performed with linear stepwise regression utilizing SPSS statistical software [SPSS Ltd, version 11, Chicago, Illinois, USA].

Results

The senior author has performed 146 transrectal ultrasounds on 107 patients with symptomatic Crohn's disease in the past decade. Between February 1994 and June 2003 67 patients with perianal Crohn's disease and symptomatic fistulae were referred for consideration of surgery to the senior author. Twenty-eight patients, with a total of 43 fistulae, were managed with long-term indwelling setons or mushroom catheters. The median age was 36 years (range
There were 20 females. The median time between diagnosis of Crohn's disease and the treatment of the fistula in this series was 3 years (range 0-17 years).

There were 5 high intersphincteric, 10 trans-sphincteric, 19 suprasphincteric, 5 extra-sphincteric and 4 rectovaginal fistulae (Figure 1). Eight patients had large abscess cavities identified on the pre-operative transanal ultrasound. Four of these had suprasphincteric fistulae and four had extra-sphincteric fistulae communicating with the abscess cavity. All eight underwent insertion of a depezzar catheter as planned pre-operatively. The remaining fistulae (n = 34) were managed with seton drainage.

Figure 1: Incidence and Type of Fistulae Using Park's Classification (RV - Rectovaginal, HIS - High Intersphincteric, LIS - Low Intersphincteric, TS - Transsphincteric, SS - Suprasphincteric, ES - Extrasphincteric)

Peri-operative, adjuvant therapy for the perianal Crohn's was used in nine patients. Only one patient was treated with both infliximab and interleukin 2.
One patient had received infliximab 12 months prior to this presentation for peri-anal Crohn’s disease. A total of five patients were receiving prednisone and or imuran at the time of the surgery. Metronidazole was used peri-operatively in nine patients and two patients were concomitantly treated with ciprofloxacin. The use of adjuvant medical therapy was not a significant predictor of post-operative symptom control (p > 0.62).

Twenty-five (88%) patients had an increased AWT on presentation compared with the normal range of 14.0 - 15.6 (Solomon 1995). The median thickness was 18.5mm (range 11 - 24mm). The AWT significantly reduced following seton insertion and symptom palliation to a median of 14mm (range 9 - 19mm) (p < 0.02).

At a median follow-up of 13 months (range 2 - 81 months, mean 21) 26 patients reported an improvement in their perianal symptoms. One patient had undergone an abdomino-perineal excision (APE) for uncontrolled sepsis one month after seton insertion. The other patient is considering a diverting stoma for poorly controlled perianal disease. This patient had previously undergone multiple small bowel resections followed by an ultra-low anterior resection and colo-anal colonic J pouch for poorly controlled ileal and rectal Crohn's disease and refusal for a permanent stoma before developing severe perianal Crohn’s disease.

Six patients (21 percent) developed recurrent or new perianal symptoms while the seton was in situ. Five of these patients had suprasphincteric fistulae at the initial procedure. The sixth patient had a transsphincteric fistula. Three patients had been on adjuvant medical therapy for their perianal Crohn's disease at the time of the first procedure. The mean time to recurrent or new symptoms was 20 months (range 1-42 months). Four patients had new tracts identified on peri-operative ultrasound. Two patients had recurrent ischiorectal abscess formation. The only patient to develop symptoms in under six months following the initial surgery was found to have a new rectovaginal fistula.
Three patients (11 percent) required a total of five further surgical interventions to drain sepsis and reposition the seton. Five courses of metronidazole in four patients only were prescribed to treat recurrent perianal sepsis.

In 5 patients (18 percent) the long-term drains fell out at a median 58 months (range 6 - 70). In 2 patients (40 percent) the symptoms of perianal sepsis recurred.

Of the 27 patients with gastrointestinal continuity no patient reported deterioration in faecal continence following seton insertion.

On univariate analysis of symptom control at the time of follow-up, younger age, lower baseline AWT and a greater reduction in AWT were all significant. On multivariate analysis younger age and a greater reduction in AWT and longer follow-up were all independently significant as predictors of symptom control (Table 1).

<table>
<thead>
<tr>
<th>Patient Factor</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Younger Age</td>
<td>0.02</td>
<td>0.005</td>
</tr>
<tr>
<td>Gender</td>
<td>0.44</td>
<td>0.25</td>
</tr>
<tr>
<td>Fistula classification</td>
<td>0.45</td>
<td>0.9</td>
</tr>
<tr>
<td>Greater AWT (at presentation)</td>
<td>0.04</td>
<td>0.09</td>
</tr>
<tr>
<td>Longer Follow-up</td>
<td>0.28</td>
<td>0.03</td>
</tr>
<tr>
<td>No. Procedures</td>
<td>0.44</td>
<td>0.1</td>
</tr>
<tr>
<td>Adjuvant medical treatment</td>
<td>0.62</td>
<td>0.44</td>
</tr>
<tr>
<td>Greater AWT reduction</td>
<td>0.02</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Table 1. Univariate and Multivariate Analysis of Symptom Control. p values provided.

Discussion

As there is currently no cure for Crohn's disease, symptom palliation without morbidity is the primary objective of treatment. For complex perianal Crohn's fistulae not responding to medical treatment the literature reports symptom control in 61 percent of patients managed with advancement flaps (Marchesa 1998), 71 percent of patients managed with fistulotomy (Bayer 1994) and less than 50 percent of patients managed with faecal diversion (Burman 1971). For each of these procedures the proctectomy rate required to finally palliate
symptoms is greater than 23 percent (Marchesa 1998). In many series the proctectomy rate is greater than 50 percent (Schwartz 2002, Sangman 1996). Only one patient (4 percent) in our series has required an APE and this was following a very short attempt by the patient at symptom control with seton placement. Our impression in this series is symptom control usually takes up to 3 months to achieve. White et al reported a small series of patients with complex perianal Crohn's fistulae managed with long-term indwelling seton (White 1990). Despite having a 60 percent incidence of severe rectal Crohn's disease they report a 100 percent success in symptom control. A larger series reported by Takesue et al. documented symptom control in 87 percent of patients (Takesue 2002). Our results also suggest that seton drainage may abate the need for proctectomy in some patients.

The role of surgical intervention in the deterioration of patient continence is controversial. Williams proposed that aggressive surgical intervention rather than the disease was responsible for the deterioration (Alexander-Williams 1980). Van Dongen et al. observed that deterioration in continence occurred in fistula patients without surgical intervention (van Dongen 1986). Studies describing aggressive surgical intervention in high, complex, perianal fistulae have reported deterioration in continence (Williams 1991). Our results, like previous studies, suggest that long-term indwelling setons do not impact on faecal continence (Bayer 1994, Marchesa 1998, Takesue 2002). However whether patient reported faecal incontinence as opposed to faeculent or mucoid fistula drainage is accurate has never been objectively assessed.

Anal wall thickness, as determined with TRUS, has previously been shown to correlate with Crohn's disease activity (Solomon 1996). Our results suggest that control of local sepsis following seton placement results in a reduction in AWT and that this reduction is an independent variable for the prediction of treatment outcome. While most patients had exhausted medical options before surgery, following seton placement many of the patients also had a change in systemic therapy and this may have been responsible for some reduction in AWT rather than the placement of the seton. However, whether the systemic or local
treatment was responsible for the reduction, AWT is one easily assessable
clinical parameter, which may predict ongoing symptom control.

Increasing patient age has not been previously reported to be associated with a
suggest that in older patients presenting with perianal Crohn's fistulae,
consideration may need to be given for earlier definitive surgical intervention.

Setons are reported to prevent recurrent suppuration (Parks 1976). However,
the recurrence of perianal sepsis with the seton insitu is still reported to be
between 23 and 44 percent (Koganei 1995, Reguiro 2003). In our series 25
percent of patients developed recurrent sepsis with the seton insitu. Fistula
recurrence following planned or inadvertent seton removal is reported to be
between 30 and 40 percent (Marchesa 1998, Faucheron 1996). Our results of
40 percent are consistent with these reports. Unfortunately many series do not
document the type of material employed as the seton. It may be that the
silicone setons as used in this series have a lower recurrence of septic
complications as a result of its monofilament, inert characteristics but these
same characteristics could delay fistula healing and therefore increase fistula
recurrence following seton removal. Unfortunately there is little published data
comparing fistula healing and recurrence rates using different seton material.

**Conclusion**

Long-term indwelling seton is an effective management modality for complex
perianal Crohn's fistulae, and appears to decrease the need for temporary or
permanent stomas. Clinical symptoms and course are inversely related to anal
wall thickness as measured on endorectal ultrasound.
CHAPTER 4

PELVIC FLOOR DYSFUNCTION

RECTOCOELE

4.1 Laparoscopic or transanal repair of rectocele? A retrospective matched cohort study


abstract published in ANZ. J. Surg. 2004; 74 (suppl) A30-A41 (CR 42P)]

4.2 Bowel, bladder and sexual function in women undergoing laparoscopic posterior compartment repair in the presence of apical or anterior compartment dysfunction.

4.1 Laparoscopic or transanal repair of rectocele? A retrospective matched cohort study

Abstract

Purpose: The aim of the study was to analyze the functional and physiological outcome of patients undergoing a laparoscopic rectocele repair compared to a matched cohort having a transanal repair.

Methods: 40 patients with a rectocele who had undergone a laparoscopic pelvic floor repair by a laparoscopic gynaecologist were matched for age and rectocele size with 40 patients who had undergone a transanal repair by a colorectal surgeon. All patients had clinical evidence of a symptomatic rectocele. All patients were assessed post-operatively with a quality of life (SF-36) score, a modified St Mark's continence score, a urinary dysfunction score, a Watt's sexual dysfunction score and a linear analogue patient satisfaction score. Fifteen patients in each group had also undergone pre and post-operative anal manometry.

Results: At 44 months median follow-up, the transanal approach resulted in significantly more patients reporting bowel symptom alleviation (p<0.002) and higher patient satisfaction scores(p<0.003). The bowel symptom improvement was also sustained over a significantly longer period (p<0.03). Only 11 patients (28 percent) in the laparoscopic group reported a greater than 50 percent improvement in their bowel symptoms compared to 25 patients (63 percent) in the transanal group. On univariate analysis of 50 percent bowel symptom improvement a larger rectocele(p<0.009), transanal repair (p<0.02) and presenting with obstructive defecation rather than faecal incontinence (p<0.03) were statistically significant. Rectocele size (p<0.012) and treatment cohort (p<0.006) remained significant on multivariate analysis. Post-operatively, bowel symptom improvement correlated with patient satisfaction in both groups (p<0.015). Although not statistically significant 5 patients (13 percent) in the transanal group developed post-operative faecal incontinence which was associated with a low maximum resting anal pressure.
(MRAP) pre-operatively and a further post-operative decline in MRAP (p>0.06). Only one patient (3 percent) in the laparoscopic group reported a decline in faecal continence but four patients (10 percent) reported a worsening of their symptoms of obstructed defecation. Post-operative dyspareunia was reported by 24 patients (30 percent), with significantly more patients in the transanal group (p>0.05).

**Conclusion:** The transanal repair results in a statistically greater improvement in bowel symptoms and higher patient satisfaction scores. However, this approach may result in a greater degree of functional morbidity than the laparoscopic rectocele repair.
Introduction

A rectocele is a posterior vaginal wall prolapse which is present to some degree in over 40 percent of women. However, a rectocele will be present in only 25 percent of patients with symptoms of a defecation disorder. Several surgical techniques are currently advocated for the repair of a clinically significant rectocele (Goh 2002, Watson 1996, Khubchandani 1983, Graul 2001, Watson 1996). The best method continues to be debated (Khan 1998, Boccasanta 2001). The transanal repair is reported to improve disordered defecation in 30-90 percent of patients (Murthy 1996, Khubchandani 1997, Tjandra 1999). It has also been noted that the surgical result deteriorates by 50 percent at 48 months post-operatively (Tjandra 2001). Furthermore, the recognised morbidity includes a 4-29 percent deterioration in fecal continence (Murthy 1996), a 20-40 percent dyspareunia rate (van Dam 2000) and a three percent rectovaginal fistula rate (Sehapayak 1985). Recently there has been increasing interest in fascial specific repairs (Singh 2003, Porter 1999). The laparoscopic approach aims to repair the fascial defects observed from above the pelvic floor (Steiner 1998). There is currently little data available on the outcome of the laparoscopic repair of clinically significant rectoceles, nor a comparison with the transanal approach (Paraiso 1999, Lyons 1997). The aim of this study is to present the post-operative outcome of a matched cohort of patients who have undergone either a transanal or laparoscopic repair of a symptomatic rectocele.

Methods

Forty patients with a symptomatic rectocele who had undergone a laparoscopic pelvic floor repair were reviewed. These patients were matched for age at the time of surgery and rectocele size with 40 patients who had undergone a transanal repair for a symptomatic rectocele.

All patients (n=80) had a clinical examination confirming the presence and size of the rectocele prior to surgery. The rectocele was considered clinically significant if the patient reported symptoms of obstructed defecation, including
the need to assist defecation with the use of either perineal or posterior vaginal pressure. All patients in the transanal group (n=40) also underwent a defecating proctogram. The radiological criteria for a significant rectocele required a defecating proctogram demonstrating a rectocele which failed to completely empty with defecation. Rectocele size was categorised into 3 groups based upon the clinical assessment of the A-P dimensions and defecating proctogram when performed. [Table 1]

**Table 1: Pre-operative patient factors**

<table>
<thead>
<tr>
<th>Factor</th>
<th>All n=80</th>
<th>Transanal n=40</th>
<th>Laparoscopic n=40</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median)</td>
<td>60 (36-81)</td>
<td>58 (36-81)</td>
<td>60 (44-76)</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td>Rectocele Size -AP</td>
<td></td>
<td></td>
<td></td>
<td>&gt;0.24</td>
</tr>
<tr>
<td>Small (1-2cm)</td>
<td>12 (15%)</td>
<td>4 (10%)</td>
<td>8 (20%)</td>
<td></td>
</tr>
<tr>
<td>Moderate (2-4cm)</td>
<td>47 (59%)</td>
<td>23 (57.5%)</td>
<td>22 (55%)</td>
<td></td>
</tr>
<tr>
<td>Large (&gt;4cm)</td>
<td>23 (28%)</td>
<td>13 (32.5%)</td>
<td>10 (25%)</td>
<td></td>
</tr>
<tr>
<td>Obstetric injury</td>
<td>61 (78%)</td>
<td>27 (68%)</td>
<td>34 (85%)</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td>Prior Hysterectomy</td>
<td>53 (66%)</td>
<td>25 (63%)</td>
<td>28 (70%)</td>
<td>&gt;0.38</td>
</tr>
<tr>
<td>HRT</td>
<td>30 (38%)</td>
<td>18 (45%)</td>
<td>12 (30%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>No</td>
<td>39</td>
<td>21</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Premenopausal</td>
<td>11</td>
<td>1</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Sexually active</td>
<td>39 (49%)</td>
<td>12 (30%)</td>
<td>27 (68%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obstetric injury</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incontinence</td>
<td>17 (21%)</td>
<td>7 (18%)</td>
<td>10 (25%)</td>
<td>&gt;0.27</td>
</tr>
<tr>
<td>Obstructed</td>
<td>63</td>
<td>23</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Urinary Symptoms</td>
<td>49 (61%)</td>
<td>15 (38%)</td>
<td>34 (85%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Genital Prolapse</td>
<td>32 (40%)</td>
<td>1 (3%)</td>
<td>31 (78%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Primary Problem</td>
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<td>&lt;0.001</td>
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<tr>
<td>Prolapse</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rectocele</td>
<td>50 (63%)</td>
<td>36 (90%)</td>
<td>14 (35%)</td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>30</td>
<td>4</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>MRAP cmH2O</td>
<td>91 (54-132)</td>
<td>87 (26-185)</td>
<td></td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Squeeze cmH2O</td>
<td>108 (26-181)</td>
<td>89 (10-264)</td>
<td></td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Cough cmH2O</td>
<td>122 (76-132)</td>
<td>104 (19-201)</td>
<td></td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>PNTML sec</td>
<td>2.3</td>
<td>2.3</td>
<td></td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Rectal Sensitivity</td>
<td>7.0</td>
<td>6.2</td>
<td></td>
<td>&gt;0.1</td>
</tr>
</tbody>
</table>

Fifteen patients in each group had also undergone pre and post-operative anorectal manometry. The anorectal manometry was performed with a six channel, low compliance, water-perfusion system, as previously reported (Kennedy 1999). Pudendal nerve terminal motor latency (PNTML) performed with a St Mark’s electrode and anal mucosal electrosensitivity studies were performed with a urethral ring electrode.
Our operative approach to the laparoscopic rectocele repair involves open laparoscopy as previously described (Lam 1997). All patients had an enema pre-operatively. Intravenous antibiotics were administered upon induction of anaesthesia. Dissection of the posterior compartment begins with uterine or vaginal vault elevation to display the utero-sacral ligaments. The ureters are identified transperitoneally and an incision is made in the peritoneum medial to the ureters. Further dissection is performed medial to the utero-sacral ligaments into the para-rectal space until the superior fascia of the levator ani muscle is exposed. In the midline the dissection is performed into the rectovaginal space from the uterosacral junction to expose the posterior vaginal wall down to the perineal body. The fascial defect resulting in the rectocele is repaired by re-attachment of the posterior vagina bilaterally to the superior fascia of the levator ani, from the perineal body to the utero-sacral ligament, using a 2/0 Ethibond Excel [Ethicon Endosurgery, Ryde, New South Wales, Australia]. The utero-sacral-cardinal ligaments are then plicated using a 2/0 ethibond suture, to the vaginal fornix or the pubocervical fascia to reconstruct the vaginal vault. Patients commenced a fluid diet on day 1 post-operatively. Antibiotics were not routinely given.

Our operative approach to the transanal repair involves making a longitudinal incision in the anterior rectal mucosa from above the dentate line to the level of the vaginal vault as assessed by intra-operative vaginal examination. A mucosal strip is excised along the length of the rectocele. A single continuous 0 vicryl suture is used to suture the mucosal edges together with the underlying muscle. The redundant rectovaginal septum is further plicated using the same continuous 0 vicryl suture. A normal diet and regular normacol [Norgine Ltd, Middlesex, UK] are commenced post-operatively and the patients are discharged the day following surgery.

The case notes and operative report were reviewed retrospectively. For the purpose of the study, each patient completed a telephone questionnaire, administered by an independent blinded observer. Bowel function was assessed with the modified St Mark's continence score (Malouf 2000). Quality
of life was assessed with the SF-36 (Ware 1992). The standard SF-36 questionnaire was administered and the final score was categorized into three quality of life categories. Essentially, level 1 were active independent patients without a medical or functional co-morbidity which impacted on their daily activities. Level 2 patients had a medical or functional co-morbidity with impacted upon but did not prevent daily activities. Level 3 had co-morbidity which significantly restricted daily activities. Sexual function was assessed with the Watt's sexual function score (Watts 1996). This score assesses the frequency and subjective quality of sexual function. The end-points specifically compared between the treatment cohorts were dyspareunia and vaginal lubrication. Patient satisfaction was assessed with a linear analogue scale. Fifteen patients in each group underwent post-operative anorectal physiology. Approval for this study was granted by the local human institutional ethics committee. All patients were informed of the aims of the study and gave consent.

**Statistical Analysis**

The Statistical Package for Social Sciences [SPSS Ltd, version 11, Chicago, Illinois, USA] was used for data analysis. Continuous data was tested for statistical significance using a two-tailed Student's t-test. Chi-squared was applied for sub-group analysis where the cohort size prevented application of the t-test. A p value <0.05 was considered statistically significant. Univariate and multivariate analysis was performed with linear stepwise regression utilising SPSS statistical software. Correlation coefficients were calculated with the Pearson's log rank coefficient.

**Results**

The median age of the combined cohorts was 60 (41-78 years). Although the groups were only matched for age and rectocele size, many of the factors known to impact on pelvic floor function did not significantly differ between the groups [Table 1]. However, the frequency of urogenital dysfunction at the time of presentation was significantly different (p<0.01). There was also a significant
difference in the hormonal status (p<0.01) and sexual activity (p<0.001) of the patients at the time of follow-up.

At a median follow-up of 44.5 months (2-179 months) there was a significant difference between the groups in terms of improvement of bowel symptoms post-operatively [Table 2].

**Table 2: Post-operative outcome**

<table>
<thead>
<tr>
<th>Factor</th>
<th>All n=80</th>
<th>Transanal n=40</th>
<th>Laparoscopic n=40</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOF (median)mths</td>
<td>44.5</td>
<td>76(16-179)</td>
<td>20(2-82)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>QOLLevel 1</td>
<td>51</td>
<td>25</td>
<td>26</td>
<td>&gt;0.9</td>
</tr>
<tr>
<td>Level 2</td>
<td>19</td>
<td>10</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Level 3</td>
<td>10</td>
<td>5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Bowel Improvement (median) 0-10</td>
<td>0</td>
<td>5</td>
<td>0</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>(mean)</td>
<td>3</td>
<td>5</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>50% Bowel improvement</td>
<td>33</td>
<td>22</td>
<td>11</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Continence score (median/24)</td>
<td>0</td>
<td>0(0-24)</td>
<td>4(0-24)</td>
<td>&lt;0.014</td>
</tr>
<tr>
<td>(mean/24)</td>
<td>5</td>
<td>3</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Time to symptom deterioration (median) mths</td>
<td>12</td>
<td>36</td>
<td>11</td>
<td>&lt;0.03</td>
</tr>
<tr>
<td>Dyspareunia</td>
<td>24 (30%)</td>
<td>15 (36%)</td>
<td>9 (22%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Vaginal Dryness</td>
<td>28 (35%)</td>
<td>13 (33%)</td>
<td>14 (35%)</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td>MRAP cmH2O</td>
<td>74(49-130)</td>
<td>91 (27-160)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squeeze cmH2O</td>
<td>80(64-181)</td>
<td>94 (14-169)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough cmH2O</td>
<td>94(75-132)</td>
<td>104(32-187)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PNTML sec</td>
<td>2.2</td>
<td>2.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rectal Sensitivity mHz</td>
<td>8.3</td>
<td>6.9</td>
<td></td>
<td>&gt;0.78</td>
</tr>
<tr>
<td>Satisfaction &gt;50%</td>
<td>50</td>
<td>25</td>
<td>25</td>
<td>&gt;0.25</td>
</tr>
<tr>
<td>Yes</td>
<td>48</td>
<td>25</td>
<td>23</td>
<td></td>
</tr>
</tbody>
</table>

Only 11 patients (28 percent) in the laparoscopic group reported 50 percent or greater improvement compared to 25 patients (63 percent) in the transanal group (p<0.02). There was also a significant difference in the degree of improvement between the groups (p<0.002)[Fig.1]. Using a linear analogue score on a scale from zero to 10, the laparoscopic group scored a median improvement of zero and a mean of 2. The transanal group scored a median and mean improvement of 5. Comparing those patients within the laparoscopic group who reported their defecation disorder as the primary problem and those who reported mixed symptoms, there was no significant difference in bowel symptom improvement (p>0.2). Within the laparoscopic group 10 percent
reported a deterioration in the symptom of obstructed defecation and 3 percent reported a decline in anal continence. No patient in the transanal group reported a deterioration in the symptom of obstructive defecation but 13 percent reported a decline in anal continence. A significantly greater number of patients in the transanal group also reported post-operative dyspareunia than in the laparoscopic group (p<0.05).

![Fig 1: 95% confidence intervals for degree of bowel improvement dependent upon treatment cohort](image)

On univariate analysis of 50 percent bowel symptom improvement a larger rectocele (p<0.009), transanal repair (p<0.02) and presenting with obstructive defecation rather than fecal incontinence (p<0.03) were statistically significant. Rectocele size (p<0.012) and treatment cohort (p<0.006) remained significant on multivariate analysis.

Over time 56 percent of patients across both groups reported deterioration in the initial improvement in post-operative bowel function. Overall, the median interval from surgery to symptomatic decline was 12 months but those patients in the transanal group experienced a significantly longer period of improvement of 36 months (p<0.003). [Fig.2]
Fig 2: Length of follow-up (LOF) marking patients with 50% improvement in bowel symptoms.

Across the groups the degree of initial bowel improvement correlated with patient satisfaction (p<0.02). In the laparoscopic but not the transanal group satisfaction levels decreased as bowel function deteriorated such that, despite the mixed presenting symptoms in the laparoscopic group, bowel symptom improvement alone correlated with patient satisfaction (p<0.001). Despite the difference in bowel symptom improvement and patient satisfaction between the treatment cohorts, there was no difference in the number of patients who would agree to the same surgical treatment a second time (p>0.2).

In neither group did pre-operative anal sphincter pressures correlate with the post-operative bowel symptom improvement (p>0.4). Although not statistically significant, in the transanal group, a low MRAP pre-operatively and further decline post-operatively were associated with a deterioration in anal continence post-operatively (p>0.06). There was also a 17 percent reduction in post-operative MRAP in the transanal group which was statistically greater than for the laparoscopic group (p<0.02) Fifty percent of patients in both groups had a prolonged PNTML pre and post-operatively. Neither pre-operative PNTML nor rectal sensitivity correlated with bowel symptom improvement (p>0.6).
Discussion:

A rectocoele is believed to be a defect in the rectovaginal fascia (Milley 1969) but the pathophysiology of the defect and the best method of repair remain areas of controversy. Consistent with our results, the transanal approach has been reported to achieve symptomatic improvement in over 60 percent of patients in the short-term (Porter 1999, Ayabaca 2002, van Dam 2000). Although our results dispute the recently published concerns that the long-term results of the transanal approach are disappointing (Tjandra 2001) over the past five years, there have been a number of new techniques proposed for rectocoele repair (Graul 2001, Maria 2001), suggesting a degree of discontent with the previously accepted methods. The laparoscopic approach is one such method, designed to address the specific fascial defects seen from above the pelvic floor (Porter 1999). Reports of the surgical outcome however are scarce and currently there is no comparative data.

There are several matching flaws in the current study. Firstly, there was a different diagnostic method used in the two cohorts. This is a common problem in the literature and as in this series is the result of the different subspecialist to whom the patient is referred (Goh 2002). The significance of this difference is difficult to assess given that at least the defecographic parameters used to confirm the presence of a significant rectocoele in the transanal repair group have been suggested to have no correlation with the clinical outcome following surgery (van Damm 1997). Similarly, a reduction in the size of the rectocoele post-operatively on defecating proctogram has not been shown to correlate with clinical improvement (van Laarhoven 1999).

The second matching flaw was the difference in the length of follow-up after surgery. The transanal cohort were required to recall pre-operative and post-operative symptoms over a thirteen year period. As the median follow-up for the laparoscopic group was only 20 months, the comparative statistics may have been subject to recall bias. However, given that the deterioration could be expected to be greater over the longer period and therefore the duration of
poorer symptoms to be greater, it may be anticipated that the lead-time bias would favour the laparoscopic group. This was not the case, suggesting that the statistically better outcome in the transanal group is valid. Furthermore, our long-term results were consistent with the intermediate-term outcomes published in the literature (Tjandra 2001).

The third matching flaw was the difference in the symptoms reported pre-operatively. Ninety percent of the laparoscopic cohort reported symptoms consistent with global pelvic floor dysfunction and as such may represent a pathologically different entity to the transanal group, 90 percent of whom had posterior pelvic floor compartment symptoms only. However, of the factors known to be associated with pelvic floor dysfunction including the incidence of prior pelvic surgery, pudendal neuropathy and obstetric trauma did not differ between the treatment groups (Kamm 1994, Vaizey 1997, Kunskar 2000). The type and frequency of bowel symptoms and pre-operative anorectal physiology was also statistically similar, suggesting that at least for the posterior pelvic floor compartment, the groups were functionally similar. Furthermore, subgroup analysis within the laparoscopic group of patients with primarily bowel symptoms did not find their outcome to be significantly different from the group with primarily mixed symptoms (p>0.2). We concede that the laparoscopic surgery performed to address urogenital dysfunction may have impacted upon the results of the rectocoele repair. Consistent with this a previous study of laparoscopic rectocele repair for patients with symptoms isolated to defecation dysfunction reported a greater improvement in defecation symptoms than our results for global pelvic floor repair (Paraiso 1999, Lyons 1997). Currently however, many women presenting to the gynaecology services will have symptoms consistent with global pelvic dysfunction and the laparoscopic approach continues to be utilized in an attempt to address the presenting dysfunction (Steiner 1998, Meshia 2002, Olsen 1997).

The reported anorectal physiology results following a rectocele repair are inconsistent. Ayabaca reported normal pre-operative resting and squeeze pressures with a 96 percent pudendal neuropathy rate in patients presenting for a transanal or transperineal rectocele repair (Ayabaca 2002). Post-operatively an insignificant increase in both resting and squeeze pressures was noted. In
contrast van Damm reported a significant decline in anal resting and squeeze pressures following a transanal repair, of which the latter did not improve over time (van Dam 2000\(^2\)). Neither study demonstrated a correlation between the manometric results and symptomatic improvement. In support of Ayabaca’s study we did not find that PNTML had a significant impact on the surgical outcome. We did however document a significant decline in anal resting pressures in the transanal group. It is hypothesised that the reduction in anal pressures is secondary to the degree of anal dilatation required to achieve the transanal repair (Kennedy 2002). However, in this cohort other factors may have been significant. There was a 7-12 year delay between the surgery and the post-operative manometry. In a cohort, with a median age of 73, a deterioration in anal manometry could have been expected during the follow-up period (Vaizey 1997). However, although the association between a low pre-operative resting anal pressure and the development of post-operative faecal incontinence did not reach statistical significance, this may be one factor to consider prior to choosing the surgical approach (van Dam 2000, Johansson 1992, van Dam 1996).

The frequency of post-operative dysparuenia reported in this study is consistent with previous reports (van Dam 2000) and although the dyspareunia rate is significantly lower in the laparoscopic group, the total number of patients affected by this morbidity was high. The rate of dyspareunia remains high irrespective of the surgical technique. Dissection of the rectovaginal septum is common to all procedures. Fibrosis consequent to this dissection may be responsible. In the laparoscopic group the change in the tension in the fascial planes as specific defects are repaired may be another factor. Further studies are required.

As may have been expected, there was a statistically significant increase in patient satisfaction with a post-operative successful outcome (Rosen 2002). However neither the degree of improvement, nor patient satisfaction was reflected in the post-operative quality of life scores. The quality of life score did not predict a successful outcome in either cohort. This held true even for those patients who developed post-operative faecal incontinence. This is not
consistent with previous studies (Wexner 2002). It may be that pre and post-operative scores would have demonstrated individual changes. For the laparoscopic group, repair of the other pelvic floor defects may have improved the quality of life score, masking the impact of the ongoing defecation disorder. However as patient satisfaction only correlated with an improvement in the defecation disorder this seems unlikely. The results remain difficult to explain.

**Conclusion**

A randomised control trial is required to minimise the matching flaws inherent in this study design. However, our results suggest that patients with a clinically significant rectocoele, treated with a transanal repair, will have a significantly greater degree of bowel symptom improvement, sustained over a significantly longer period than patients treated laparoscopically. Furthermore our results suggest that patients with a larger rectocoele and symptoms of obstructive defecation are more likely to benefit from the repair.
4.2 Bowel, bladder and sexual function in women undergoing laparoscopic posterior compartment repair in the presence of apical or anterior compartment dysfunction.

Abstract

Objective: The aim of the study was to analyse the functional outcome of women undergoing a laparoscopic posterior compartment repair in the presence of anterior or apical compartment dysfunction.

Methods: 40 women, median age 65 years (41-78), 31(78 percent), 32 (80 percent) and 40(100 percent) with symptoms of genital prolapse, urinary and bowel dysfunction, underwent laparoscopic posterior compartment repair in conjunction with an anterior compartment repair. Pre-operative and post-operative bowel and bladder function was prospectively assessed with a Wexner continence score, Vienna constipation score and a urinary dysfunction score. Twenty-eight (70 percent) and 24 patients (60 percent) had pre-operative urodynamics and anorectal manometry. Post-operatively all women were also assessed with a Watt's sexual dysfunction score and a linear analogue patient satisfaction score. Twelve women (30 percent) had post-operative anal manometry.

Results: At 20 months median follow-up, 30 (97 percent), 20 (62 percent) and 12(31 percent) women reported improvement in their prolapse, urinary and bowel symptoms respectively. Post-operatively, one woman reported denovo faecal incontinence, four worsening obstructive defecation and three denovo urinary dysfunction. Nine women (35 percent) reported denovo dyspareunia. The mean time to clinical deterioration following surgery was 11 months. Bowel function improvement was the only factor to significantly correlate with post-operative patient satisfaction.

Conclusion: The functional outcome of laparoscopic posterior compartment repair in the presence of anterior compartment dysfunction is disappointing. Preoperative counselling is important to ensure that patients have reasonable
and realistic expectations from repair surgery, and an understanding that anatomical improvement may not be followed by long-term functional improvement.
Introduction

The pelvic floor is a single complex anatomical structure whose function is integrally related to bladder, bowel and sexual organ function. Consequently the effects of pelvic floor weakness frequently manifest as multi-organ dysfunction. By 50 years of age 30-50% of women will have more than one symptom of pelvic floor dysfunction (Steiner 1998, Meshia 2002). Overall, each woman has an 11% life-time incidence of requiring surgery for one symptom of pelvic floor weakness (Olsen 1997). Up to 24% will have concomitant symptoms of bladder, bowel and sexual organ dysfunction (Meshia 2002). There are numerous laparoscopic techniques described for treating single viscus dysfunction resulting from pelvic floor weakness (Steiner 1998, Koduri 2000, Seman 2003). The outcome for those patients with symptoms of global dysfunction has not been previously reported. The purpose of this study was to evaluate the effect on bowel, bladder and sexual function in a cohort of women who underwent laparoscopic posterior compartment repair in the presence of anterior compartment dysfunction.

Materials and methods

Between July 1997 and October 2002, 40 patients were referred with symptoms of obstructed defecation and anterior compartment dysfunction. Thirty-one (78 percent) reported symptoms of genital prolapse and 32 (80 percent) reported urinary dysfunction. Twenty-two (69 percent) reported urinary incontinence, stress or urge and 10 reported obstructive symptoms. Stress incontinence was defined as the involuntary loss of urine with exertion. Urge incontinence was defined as the inability to defer micturition for longer than five minutes after the urge to void. Obstruction was defined as the need to strain to initiate micturition combined with the sensation of incomplete emptying. Eleven women also reported faecal incontinence, as defined by involuntary leakage of solid or liquid stool or the inability to defer defecation for five minutes after the call to evacuate.
All patients had a pre-operative evaluation that included a full history, a Wexner continence score (appendix 2, Jorge 1993), a Vienna constipation score (appendix 3, Altomare 2002) and a urogenital distress inventory (Uebersax 1995). Patients also completed a linear analogue assessment of bowel, bladder and genital symptoms. Subjective bowel and bladder control was graded from zero, being no control, to ten, being perfect control. The sensation of a perineal bulge or discomfort was graded from zero, being never present, to ten, being present on a daily basis. Patients also completed a linear analogue scale of the frequency which their bowel, bladder and prolapse symptoms prevented normal daily activities, with zero being always able to perform daily activities, to ten, being prevented from performing normal activities on a daily basis.

A systematic site-specific pelvic examination, first at rest and then with maximum straining, in the supine and standing positions was then performed. Pelvic organ prolapse was graded according to the Baden-Walker classification (Baden 1972). All women had clinical evidence of genital prolapse and a clinically significant rectocele as defined by clinical symptoms of obstructed defecation and a posterior vaginal bulge.

Twenty-eight women (70%) underwent multi-channel urodynamic investigation that included uroflowmetry, subtracted cystometry, transvaginal ultrasound assessment of the bladder neck or videocystometrogram, and where indicated urethral pressure profile. Urodynamic evidence of stress incontinence was based on a leak point pressure of 60 centimetres of water. Evidence of bladder outlet obstruction was defined as a maximum flow of less than 15ml per second with maximum detrusor pressure of greater than 25 cm of water.

Twenty-four women (60%) underwent anorectal manometry which included a six channel, low compliance, water-perfusion system, as previously reported (Kennedy 1999). Pudendal nerve terminal motor latency (PNTML) and rectal sensitivity studies were performed with a St Mark’s electrode. Patient consent and resource availability prevented full compliance with anorectal manometry and urodynamic investigation.
All women gave informed consent to the surgical procedure including the laparoscopic posterior compartment repair. An enema was given preoperatively. Intravenous antibiotics were administered upon induction of anaesthesia. Open laparoscopy was performed as previously described (Lam 1997). For the posterior compartment repair, dissection begins with uterine or vaginal vault elevation to display the utero-sacral ligaments. The ureters are identified transperitoneally and an incision is made in the peritoneum medial to the ureters. Further dissection is performed medial to the utero-sacral ligaments into the pararectal space until the levator ani muscle superior fascia is exposed. In the midline, the dissection is made into the rectovaginal space from the uterosacral junction to expose the posterior vaginal wall down to the perineal body.

The level of the pelvic floor repair performed was graded by DeLancey's classification (DeLancey 1992). The Delancey level 2 defects resulting in a rectocoele are repaired by re-attachment of the posterior vagina bilaterally to the levator ani superior fascia, from the perineal body to the uterosacral ligaments, using on average 4 interrupted 0-Ethibond sutures on a 26 mm taper cut CT-2 needle (Ethicon Endosurgery, Ryde, New South Wales, Australia). The level 1 repair involves plication of the uterosacral- cardinal- ligaments to the vagina fornix and cervix (where uterus was still present) or to the pubocervical fascia and the vaginal angles in post-hysterectomy patients to reconstruct the vaginal vault.

In women with anterior vaginal wall prolapse and/or urinary incontinence, a laparoscopic colposuspension and/or paravaginal repair was also performed. A laparoscopic anterior colporrhaphy was carried out in women with a moderate to large central cystocele. Where a deficient perineum or a very low rectocele were present, these were repaired transvaginally to complete the pelvic floor repair. A cystoscopy was performed at the end of the procedure to confirm bilateral ureteric patency and to check for bladder integrity.

Post-operatively, patients commenced a fluid diet on day 1 post-operatively. Antibiotics were not routinely given. The case notes and operative report were
reviewed retrospectively. For the purpose of the study, each woman completed a telephone questionnaire, administered by an independent observer. Bowel and bladder function was again assessed with the Wexner continence score (Jorge 1993, appendix 2) the Vienna constipation score (Altomare 2002, appendix 3) and the Urogenital Distress Inventory (Uebersax 1995). Patients repeated the linear analogue assessment of subjective bowel, bladder and prolapse symptoms. The difference between baseline and final score was calculated to provide a score for symptom improvement with zero being no improvement, to ten, being complete resolution of the pre-operative symptom. Sexual function was assessed with the Watt’s sexual function score (Watts 1996). Patient satisfaction with symptom change was assessed with a linear analogue scale. Fifteen women agreed to undergo post-operative anorectal physiology.

All protocols were approved by the South Eastern Area Health Service Ethics Committee.

Statistical Analysis

All parameters assessed pre and post-operatively were assessed with a paired t-test. A p value <0.05 was considered significant (two-tailed). Subgroup analysis was performed using the Mann-Whitney U test.

Results

At a median of 20 months [5-82 months] 40 women were available for assessment. The median age at the time of surgery was 65 (41-78). All women were parous with a median parity of 2 children. [Table 1]

Twenty-four of the 28 women pre-operatively assessed (86 percent) were found to have abnormal urodynamics. There was a statistically significant association between the pre-operative urinary symptoms, the urodynamic result and the urogenital distress inventory score (p<0.01). Thirteen of the 24 women pre-operatively assessed (54 percent) were found to have abnormal anorectal
physiology. The median pre-operative continence score was five. The mean resting and squeeze anal pressures were 84cmH₂O and 89cmH₂O respectively. There was a statistically significant negative association between the continence score and resting and squeeze anal pressures (p<0.001). Fifty percent of women had a prolonged PNTML pre-operatively (median 2.2). Rectal electro-sensitivity was normal in all women. Rectocele size had a significant positive association with the pre-operative Vienna score (p=0.029) and a significant negative association with the pre-operative Wexner score. Rectocele size was not however associated with pre-operative symptoms (p=0.253) or pre-operative physiology (p=0.356).

<table>
<thead>
<tr>
<th>Age</th>
<th>median 61 (41-78)</th>
<th>0.352</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parity</td>
<td>median 2 (1-8)</td>
<td>0.355</td>
</tr>
<tr>
<td>Perineal Injury</td>
<td>33 (83%)</td>
<td>0.602</td>
</tr>
<tr>
<td></td>
<td>tear 15, episiotomy 1, forceps 3, combination 13</td>
<td></td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>27 (68%)</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td>abdominal 20, vaginal 7</td>
<td></td>
</tr>
<tr>
<td>Post-menopausal</td>
<td>30 (75%)</td>
<td>0.528</td>
</tr>
<tr>
<td>HRT</td>
<td>12 (40%)</td>
<td>0.902</td>
</tr>
<tr>
<td>Pelvic surgery</td>
<td>15 (38%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>bladder 6, rectocele 1, genital prolapse 1, combination 4</td>
<td></td>
</tr>
<tr>
<td>Prolapse symptoms</td>
<td>31 (78%)</td>
<td>0.882</td>
</tr>
<tr>
<td>Urinary Dysfunction</td>
<td>32 (80%)</td>
<td>0.137</td>
</tr>
<tr>
<td></td>
<td>stress/urge incontinence 21, outflow obstruction 11</td>
<td></td>
</tr>
<tr>
<td>Urodynamic diagnosis</td>
<td>stress incontinence 15, detrusor instability 2, outflow obstruction 4, sensory urgency 3, normal 4</td>
<td>0.445</td>
</tr>
<tr>
<td>Bowel Symptoms</td>
<td>40 (100%)</td>
<td>0.399</td>
</tr>
<tr>
<td></td>
<td>Incontinence 11, obstructed defecation 40</td>
<td></td>
</tr>
<tr>
<td>Continenence Score</td>
<td>median 8 (0-24)</td>
<td>0.999</td>
</tr>
<tr>
<td>Rectocele Size</td>
<td>&lt;2cm 9, 2-4cm 21, &gt;4cm 10</td>
<td>0.313</td>
</tr>
</tbody>
</table>

Table 1: Pre-operative variables and their significance on univariate analysis of the bowel symptom improvement score.

Twenty-six women (65 percent) had a level 2 pelvic floor repair, ten women (25 percent) had a level 1 repair and four women (10 percent) had a level 3 repair. Concomitantly 18 women (45 percent) had a colposuspension, 11 women (28 percent) an anterior colporrhaphy, 16 women (40 percent) a posterior colporrhaphy for level III (low) rectocele and 13 women (32 percent) a perineorrhaphy. [Table 2]
Table 2: Procedures performed concomitant with and dependent on the level of the pelvic floor repair

At a median follow-up of 20 months, symptomatic improvement varied throughout the pelvic floor compartments. [Fig 1]

The linear analogue scores completed pre and post-operatively identified a median prolapse symptom improvement of eight. Thirty women (97 percent) reported some improvement in their genital prolapse symptoms. Of these, 28 (88 percent) reported greater than 50 percent improvement. There was no significant association between any of the pre-operative factors listed in Table 1, and the post-operative result. Nor was there a significant association...
between the level of the pelvic floor repair performed and the post-operative outcome.

The median bladder symptom improvement score from pre to post-operative linear analogue assessment was five. Twenty women (62 percent) reported some improvement in their urinary function. Of these, 18 (90 percent) of these women reported a greater than 50 percent symptom improvement. In keeping with this there was a significant improvement in the post-operative urogenital distress inventory score compared to the pre-operative score (p=0.031). Three women with normal pre-operative function reported denovo obstructive urinary symptoms post-operatively. A further five women with pre-operative obstructive symptoms reported a deterioration in outflow symptoms. Of the 23 women reporting no improvement or symptom deterioration, 17 (74 percent) had undergone a concomitant colposuspension or anterior colporrhaphy. This intra-operative factor was significantly associated with less than 50% improvement in urinary symptoms (p<0.001). The pre-operative factors significantly associated with less than 50 percent improvement included a prior hysterectomy and urodynamics consistent with outflow obstruction (p= 0.002, p<0.01 respectively).

The median bowel symptom improvement score from pre to post-operative linear analogue assessment was zero. Twelve women (31 percent) reported some improvement in their bowel dysfunction. Eleven of these reported a greater than 50 percent improvement. The median post-operative continence score was four. This was not statistically different to the pre-operative score. One woman reported denovo post-operative faecal incontinence and four women reported that the symptoms of obstructive defecation had worsened. Resting, squeeze pressures, PNTML and rectal sensitivity did not significantly change post-operatively (p<0.01). Pre-operative or post-operative anal sphincter pressures (p=0.9), PNTML (p=0.6) and rectal sensitivity (p=0.9) did not correlate with symptomatic improvement. Pre-operative faecal incontinence was significantly associated with less than 50 percent improvement in bowel function (p=0.04). Rectocele size was not
associated with a poorer outcome (p=0.328). There were no intra-operative factors significantly associated with less than 50% improvement.

The questionnaire assessed retrospectively symptom improvement over time. Overall, the mean time to the beginning of a deterioration in the post-operative outcome was 11 months. All symptom categories assessed significantly deteriorated over time (bowel p=0.004, urinary p=0.006, prolapse p=0.018). As the symptoms deteriorated, patient satisfaction with the operative outcome also significantly decreased (p=0.015).

**Dyspareunia**

Post-operatively 28 women (69 percent) reported that they were sexually active. Ten women (35 percent) reported that they had developed denovo dyspareunia. One patient reported that the pain was so intense that all sexual relations had ceased. No pre or intra-operative factors were associated with the development of post-operative dysparuenia, including the addition of a perineal scar.

**Patient Satisfaction**

Overall twenty-five women (62.5 percent) reported they were satisfied with the post-operative outcome. However, the only pre-operative variable or symptom outcome to correlate with patient satisfaction was the degree of bowel symptom improvement (p=0.002). As the bowel symptoms deteriorated, patient satisfaction with the operative outcome also decreased (p=0.015). Only 18 women (46 percent) reported that they would have undergone the surgery had they known the outcome. Of those patients with only pre-operative bowel symptoms less than 25 percent reported that they would agree to the same operation again to help improve their defecation disorder.

**Discussion**
There is an increasing awareness that symptoms of genital prolapse, urinary and bowel dysfunction often occur in combination and that each needs careful pre-operative assessment (Steiner 1998, Jackson 1997). However, there is little consensus as to the best method of surgical management. Often, the surgical method chosen depends upon the surgeon’s training specialty and experience. The senior author developed and adopted the laparoscopic approach to the pelvic floor for correction of posterior compartment dysfunction which is in accordance with Delancey’s anatomical description of the three levels of vaginal support and rectocele formation. This is based upon the understanding that the rectovaginal septum (RVS) has a diaphragm-like configuration, with cranial attachments to the uterosacral ligaments and the cul-de-sac peritoneum, with caudal attachments to the perineal body, and lateral attachment to the superior fascia of the levator ani muscles. Therefore, our laparoscopic approach to the pelvic floor and reconstruction of the RVS aims to reattach the LAM fascia for a level II repair, and to reconstruct the utero-sacral vault complex for a level III suspension. While the anatomical outcome would seem satisfactory as indicated by the 97% of prolapse cure rate, the improvement in bowel and to a lesser extent bladder function in our series is rather disappointing.

The improvement in urinary dysfunction documented in this study is lower than for previously described techniques (Wahle 1994, Raz 1996). Several factors may be responsible. Firstly, hysterectomy is associated with post-operative bladder and bowel dysfunction (Petros 1993, Brown 2000). Twenty-seven of our women (68 percent) had undergone a prior hysterectomy and this was a significant predictor of poorer outcome. Secondly, the surgical techniques for correcting genital prolapse following a hysterectomy are associated with post-operative urinary dysfunction (Timmons 1992, Varner 1995, Abdel-Fattah 2004). Seventeen of our women (74 percent) reporting no improvement had undergone a concomitant colposuspension or anterior colporrhaphy and all patients reporting symptom deterioration had undergone one or other procedure. Concomitant surgical intervention was a significant predictor of a poorer outcome. Finally, all patients with symptoms of urinary dysfunction had presented with symptoms of global pelvic floor weakness that is genital.
prolapse, bladder and bowel dysfunction. The laparoscopic approach was not an attempt to treat an isolated defect and as such one could anticipate that the results would not be as favourable as those studies reporting outcome following single compartment surgery (Abdel-Fattah 2004).

Several of the factors potentially responsible for the disappointing improvement in urinary symptoms are also applicable to the disappointing improvement in bowel symptoms. Hysterectomy, previously performed in 68 percent of our women, is associated with post-operative obstructive defecation in up to 30 percent of patients (Brown 2000, Smith 1990). Pelvic reconstructive prolapse surgery has also been reported to have a 26 percent incidence of denovo disordered defecation post-operatively (Virtanen 1994, Pilsgaard 1999). Fourteen women in this cohort had undergone previous reconstructive surgery. A further 16 patients (40 percent) had undergone a concomitant posterior colporrhaphy and perineorrhaphy for correction of a residual rectocoele and deficient perineum. This procedure has been shown to be associated with poor bowel functional outcome, including constipation, denovo fecal incontinence and dyspareunia (Kahn 1997).

It is possible that laparoscopic pelvic floor repair, particular division of the lateral rectal ligaments resulted in further neurovascular injury to the anorectal complex. It is hypothesised that lateral rectal dissection results in an increase in the rectal sensory threshhold which directly contributes to post-operative constipation (Mollen 2000, Speakman 1991). Similar to our results Baessler et al reported a less than 30 percent symptomatic improvement in disordered defecation with an abdominal approach to the pelvic floor for rectocele repair (Baessler 2001). The abdominal approach, laparoscopic or open, necessitates dissection of the lateral pelvic wall to enable the other elements of the pelvic floor repair. This dissection may partly explain the poorer results of the laparoscopic rectocele repair compared to the success rates of up to 70-90 percent for the transanal approach (Murthy 1996, Tjandra 1999). Although we did not demonstrate a significant change in rectal sensitivity or PTNML post-operatively the number of patients with symptomatic improvement and post-
operative anorectal physiology was too small for independent statistical comparison.

Several other factors may explain the difference in the results between the perineal, transanal or transvaginal, and the laparoscopic approach. As outlined above, the trial patients have multiple symptoms of pelvic floor weakness, rather than an isolated pelvic floor fascial defect, most have had a hysterectomy and many have had previous pelvic surgery. Although such patients are likely to be included in the perineal studies their results are not identifiable from the cohort results.

The laparoscopic repair did result in a lower rate of post-operative faecal incontinence compared to a perineal approach, transvaginal or transanal (Virtanen 1994, van Dam 2000). The increased rate of faecal incontinence following the transanal approach is believed to be secondary to internal anal sphincter damage peri-operatively (Kennedy 2002). The reason for lower incontinence rates following the laparoscopic approach compared to the transvaginal approach is unclear. It is possible that the pelvic floor repair performed laparoscopically provides additional support for the lower rectum and sphincter complex. It may also be that there is less neurovascular damage consequent upon the laparoscopic repair compared to the transvaginal repair. Further investigation is required.

Dyspareunia is commonly reported in patients undergoing pelvic surgery. Posterior colporrhaphy, as performed in 40 percent of this cohort, is associated with post-operative vaginal shortening and narrowing with a dyspareunia rate of 22 percent (Arnold 1990). Sacral colpopexy, performed in 45 percent of this cohort, is also associated with a post-operative dyspareunia rate of 9 percent (Baessler 2001, Creighton 1991). Of the 35 percent of women who reported denovo post-operative dyspareunia, 86 percent of these had undergone concomitant perineal surgery, all had undergone previous pelvic surgery. The effect of the laparoscopic component of the pelvic floor repair on sexual function could not be determined in this study.
The data on the physiological effects of pelvic floor surgery are inconsistent (Ayabaca 2002, van Dam 2000). It may be anticipated that an anatomical correction of the deficient pelvic floor will be detected in at least the manometric pressure profiles. However, as is this study, van Tets et al have reported no consistent changes in anorectal physiology following pelvic floor surgery (van Tets 1998). Our results also failed to establish a relationship between pre-operative manometry, changes in manometry and the post-operative outcome. Even the presence of pudendal neuropathy did not significantly impact on the outcome. The interplay of the mechanical and neurogenical components of the pelvic floor remains poorly understood.

Although women who undergo surgery for pelvic floor dysfunction have a variety of desired objective outcomes, symptom relief is the outcome measure most frequently given as the desired goal (Hullfish 2002). Patient satisfaction therefore becomes dependent upon symptom relief as shown in this study. Of interest however, only improvement in the defecation symptoms correlated with patient satisfaction. Improvement in the symptoms of genital prolapse or urinary dysfunction, although reported in over 60% of patients, did not correlate with patient satisfaction. Disorders of bowel function are not frequently reported by patients, even when the symptoms are severe (Woods 1998). This is likely to be a reflection of the continuing social stigma associated with defecation disorders and may be the reason why bowel symptom improvement was the symptom which correlated with patient satisfaction.

Conclusion

The functional outcome of laparoscopic posterior compartment repair in the presence of anterior compartment dysfunction is disappointing. Preoperative counselling is important to ensure that patients have reasonable and realistic expectations from repair surgery, and an understanding that anatomical improvement is not often followed by long-term functional improvement.
Bibliography


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Lindsey I, Jones OM, Cunningham C, George BD, Mortensen NJM. Botulinum toxin as second line therapy for chronic anal fissure failing 0.2 percent glyceryl trinitrate. Dis Colon Rectum 2003;46:361-366.


**Speakman** CTM. Pharmacology of the internal anal sphincter and abnormalities in faecal incontinence. European J Gastroent & Hepatol 1997;9:442-446.


van Tets WF, Kuijpers JHC. Pelvic floor procedures produce no consistent changes in anatomy or physiology. Dis Colon Rectum 1998;41:365-369.


## Appendix 1: Modified St Mark’s Continence Score

<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Rarely</th>
<th>Sometimes</th>
<th>Weekly</th>
<th>Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incontinence for solid stool</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Incontinence for liquid stool</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Incontinence for gas</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Alteration in lifestyle</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Need to wear a pad or plug</td>
<td></td>
<td></td>
<td></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Taking constipating medicines</td>
<td></td>
<td></td>
<td></td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Lack of ability to defer defecation for 15 minutes</td>
<td></td>
<td></td>
<td></td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

Never, no episodes in the past four weeks; rarely, 1 episode in the past four weeks; sometimes >1 episode in the past four weeks but <1 a week; weekly, 1 or more episodes a week but <1 a day; daily, 1 or more episodes a day.

Add one score from each row: minimum score = 0 = perfect continence; maximum score = 24 = totally incontinent.
**Appendix 2: Wexner Incontinence Score**

<table>
<thead>
<tr>
<th>Type of Incontinence times</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Never</td>
</tr>
<tr>
<td>Solid</td>
<td>0</td>
</tr>
<tr>
<td>Liquid</td>
<td>0</td>
</tr>
<tr>
<td>Gas</td>
<td>0</td>
</tr>
<tr>
<td>Wears Pad</td>
<td>0</td>
</tr>
<tr>
<td>Lifestyle Alteration</td>
<td>0</td>
</tr>
</tbody>
</table>

0 = perfect
20 = complete incontinence
Never = 0 (never)
Rarely = <1/month
Sometimes = <1/week, ≥1/month
Usually = <1/day, ≥1/week
Always = ≥1/day
### Appendix 3: Vienna Constipation Score

<table>
<thead>
<tr>
<th>Incomplete or Failed evacuation</th>
<th>Strains for &gt;30 mins</th>
<th>Enemas, irrigation digital evacuation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>I</td>
<td>I</td>
</tr>
<tr>
<td>&lt;1/week</td>
<td>II</td>
<td>II</td>
</tr>
<tr>
<td>≥1/week –</td>
<td>III</td>
<td>III</td>
</tr>
<tr>
<td>&lt;1/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1/day</td>
<td>IV</td>
<td>IV</td>
</tr>
</tbody>
</table>


### Appendix 4: Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AWT</td>
<td>anal wall thickness</td>
</tr>
<tr>
<td>BT</td>
<td>botulinum toxin</td>
</tr>
<tr>
<td>CAF</td>
<td>chronic anal fissure</td>
</tr>
<tr>
<td>CO₂</td>
<td>carbon dioxide</td>
</tr>
<tr>
<td>DGP</td>
<td>dynamic graciloplasty</td>
</tr>
<tr>
<td>EAS</td>
<td>external anal sphincter</td>
</tr>
<tr>
<td>EMG</td>
<td>electromyography</td>
</tr>
<tr>
<td>ExMI</td>
<td>extracorporeal magnetic stimulation</td>
</tr>
<tr>
<td>-fw</td>
<td>fast wave</td>
</tr>
<tr>
<td>GTN</td>
<td>glyceryl trinitrate</td>
</tr>
<tr>
<td>IAS</td>
<td>internal anal sphincter</td>
</tr>
<tr>
<td>inos</td>
<td>inducible nitric oxide</td>
</tr>
<tr>
<td>MRAP</td>
<td>maximum resting anal pressure</td>
</tr>
<tr>
<td>NO</td>
<td>nitric oxide</td>
</tr>
<tr>
<td>PNTML</td>
<td>pudendal nerve terminal motor latency</td>
</tr>
<tr>
<td>QOL</td>
<td>quality of life</td>
</tr>
<tr>
<td>RAIR</td>
<td>recto-anal inhibitory reflex</td>
</tr>
<tr>
<td>RAP</td>
<td>resting anal pressure</td>
</tr>
<tr>
<td>RVS</td>
<td>recto-vaginal septum</td>
</tr>
<tr>
<td>S</td>
<td>sacral</td>
</tr>
<tr>
<td>SW</td>
<td>slow wave</td>
</tr>
<tr>
<td>USW</td>
<td>ultra-slow wave</td>
</tr>
<tr>
<td>TRUS</td>
<td>trans-rectal ultrasound</td>
</tr>
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</table>