By all of our metrics the Congress was an outstanding success. There were 700 delegates closeted in Cairns for a week and socially and scientifically the event was peerless. I do pay tribute to energy and drive of Sally Marasco and all of the programme committee members. We started the meeting at Royal Melbourne in 2000 and it has grown from 25 delegates to 950 in Melbourne in 2013. The highlight for me was the dinner in the oil tanks just out of Cairns town proper. These tanks housed oil supplies for the Australian and US navies in the Second World War. They have now been turned into a reception centre in the rainforest.

Two of our international guests, Patrick Walsh and Bill Catalona, whom I believe are two of the most outstanding Doctors/Urologists in recent history, were interviewed. They pioneered the reduction in the morbidity of therapy and the 42% decline in US mortality from prostate cancer since the late 1980’s. It was truly spellbinding and a privilege to listen to these two men interviewed about their careers, their ethical views, and excitement for what has been achieved with early diagnosis and safe curative prostate cancer surgery.

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This week the Journal of Urology [1] published an assessment of the impact on PSA testing of the USPC taskforce recommendations against prostate cancer screening [2]. There has been a dramatic drop in prostate cancer diagnosis across all grades of cancer, including a decline in diagnosis of intermediate and high-grade disease i.e. the cancers where early diagnosis can save lives.

In 2012, the NIH [3] published the USA prostate cancer mortality decline of 42% from 1990 due to early diagnosis (PSA) and curative intervention. We do acknowledge the overtreatment of some of those patients with low risk disease who now would be placed on Active Surveillance. We know from our Victorian Registry data (personal communication) that we place 40% of men with low risk prostate cancer on Active Surveillance (2014). We are now also better informed about lethality of aggressive prostate cancer.

Already in my own practice I am seeing more advanced disease at presentation, coinciding with a decline in testing in Victoria in recent years.

If there is no diagnosis we cannot stratify for risk and allow for early intervention where appropriate and active surveillance for those who don’t need immediate treatment.

It is clearly enunciated in the Melbourne Consensus Statement on Prostate Cancer Testing, statement 3 “we must uncouple diagnosis from treatment” [4]. Not knowing whether a man has prostate cancer by doing away with PSA testing “burns bridges”.

We know mostly when and who to treat and what treatments work well [5]. To me the prostate cancer testing debate resonates with the contemporary discussion regarding childhood immunisation for infectious diseases. Some parents, who clearly cannot remember the devastating epidemics of polio and other childhood illnesses, refuse to immunise their children. Prostate cancer practitioners, who did not live in the quite recent era where the cancers where early diagnosis can save lives.

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At the recent 2013 AUA meeting Adams et al, report on the fate of men not screened for prostate cancer, i.e. those men who present with a PSA >100 [6]. There was a 9.7% three year survival, a 19.7% cord compression rate, and 44% hospitilisation rate. Those who don’t learn the lessons of history are condemned to repeat them.

References

Prostate cancer histology: moving beyond the Gleason score after 40 years
Dr Andrew Ryan
TissuPath, Mount Waverley, Victoria

Despite rarely having direct patient contact, pathologists play a crucial role in the diagnosis and management of most cancer patients. Our main responsibility is to deliver an accurate and concise report containing information about the specific type of tumour biopsied, as well as prognostic information ascertained through macroscopic and microscopic examination and ancillary testing.

Gleason grading of prostate carcinoma has been a cornerstone of prognostic information for four decades. Originally conceived by Donald Gleason in 1965, the Gleason grading system is an assessment of the architectural growth pattern of the tumour, with specific growth patterns attributed scores ranging from 1 to 5. The most common and second most common patterns are then presented as a sum score (3+4=7 means pattern 3 is the most common and pattern 4 the second most common pattern).

The Gleason grading system has been revised several times (1970’s, 2005, 2014), the most modern iteration now technically a ‘modified modified Gleason grading system’. However these modifications not only failed to address several flaws identified in the original system, but also created additional issues including:

- Use of patterns 1 and 2 have been discouraged in modern versions of the system (some of the lesions originally graded as 1 and 2 were likely lesions that we now recognise as benign). This has resulted in Gleason score 6 (3+3) being the lowest grade; seemingly not a big issue until clinicians worldwide tried to sell active surveillance to their patients who had tumours with a score of 6 out of 10!
- Artificial grouping of patients was occurring in clinical (nomogram) and research settings (eg D’Amico, 2-6, 7-10) without proper validation and without standardisation.
- With the system name maintained throughout, tumour data acquired under different iterations of the grading system was sometimes being incorrectly pooled or compared; not entirely apples and oranges, but still bad science.

With these issues in mind, a new grading system has been designed by Epstein et al. [1] (a Johns Hopkins pathologist). While the foundations of the new grading system have not changed (still based on the architectural pattern of the tumour), there has been:

- Simplification of the way tumour architecture will be assessed; tumour components to be assessed as ‘well formed glands’ (equivalent to pattern 3), ‘poorly formed or complex glands’ (equivalent to pattern 4) or ‘no gland formation’ (equivalent to pattern 5),
- A change to the way the results of the assessment are presented to the treating clinicians and their patients. Now, rather than a sum score, tumours will be classified into one of 5 ‘grade group’ (see table 1).
- A marked simplification from the 25 potential grade combinations under the old system.

<table>
<thead>
<tr>
<th>Histologic definition of new grading system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade Group 1 (Gleason Score 3 + 3 = 6)</td>
</tr>
<tr>
<td>Only individual discrete well-formed glands</td>
</tr>
<tr>
<td>Grade Group 2 (Gleason Score 3 + 4 = 7)</td>
</tr>
<tr>
<td>Predominantly well-formed glands with lesser component of poorly formed/fused/cribriform glands</td>
</tr>
<tr>
<td>Grade Group 3 (Gleason Score 4 + 3 = 7)</td>
</tr>
<tr>
<td>Predominantly poorly formed glands with lesser component of poorly formed/fused/cribriform glands</td>
</tr>
<tr>
<td>Grade Group 4 (Gleason Score 5)</td>
</tr>
<tr>
<td>Only poorly formed/fused/cribriform glands, or Predominantly well-formed glands and lesser component lacking glands</td>
</tr>
<tr>
<td>Grade Group 5 (Gleason Score 9-10)</td>
</tr>
<tr>
<td>Lack of gland formation or with necrosis with or without poorly formed/fused/cribriform glands</td>
</tr>
</tbody>
</table>

In a validation study of >20,000 men treated by radical prostatectomy and >5000 men treated with radiotherapy, this new 5 tiered system was found by Epstein et al to stratify men into clearly discernible prognostic groups based on biochemical recurrence (Fig 1). The 5 tiered system outperformed other 3 and 4 tier combinations tested, and importantly, clearly separated the often aggregated “Gleason 7” into two clearly distinct prognostic groups; grade group 2 (3+4=7) and grade group 3 (4+3=7). Stratification was demonstrated using both radical prostatectomy grading (Fig 1) and pre-prostatectomy biopsy grade, and was also demonstrated in patients receiving primary radiotherapy treatment.

The new system also has the significant benefit of presenting the lowest grade tumours as the lowest grade group (ie grade group 1) rather than as 6 on a scale of 10. It is hoped that this will contribute to continued improvement in patient acceptance of active surveillance with a subsequent decrease in the overtreatment of low-grade prostate cancer detected by prostate-specific antigen (PSA).

The new grading system has been ratified by ISUP (International Society of Urological Pathology) and will be included in the upcoming 2016 WHO Classification of tumours of the urinary system and male genital organs. It is recommended that Pathologists use the new ISUP/Epstein grade group system in conjunction with the Gleason grading system until the former is widely accepted and practiced.

References

Table 1 – Histologic definition of new grading system (reproduced from [1] with permission)

Fig. 1 – Recurrence-free progression following radical prostatectomy stratified by prostatectomy grade.

<table>
<thead>
<tr>
<th>Number at risk</th>
<th>Gleason score 6, Grade Group 1</th>
<th>Gleason score 3 + 4, Grade Group 2</th>
<th>Gleason score 4 + 3, Grade Group 3</th>
<th>Gleason score 8, Grade Group 4</th>
<th>Gleason score ≥9, Grade Group 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥5</td>
<td>7 797</td>
<td>6 973</td>
<td>5104</td>
<td>4084</td>
<td>3226</td>
</tr>
<tr>
<td>3 + 4</td>
<td>8 353</td>
<td>7 022</td>
<td>5 298</td>
<td>3 983</td>
<td>2 915</td>
</tr>
<tr>
<td>4 + 3</td>
<td>3 106</td>
<td>2 452</td>
<td>1 465</td>
<td>1 132</td>
<td>8 398</td>
</tr>
<tr>
<td>≥9</td>
<td>9 367</td>
<td>7 478</td>
<td>4 412</td>
<td>2 280</td>
<td>2 191</td>
</tr>
</tbody>
</table>

RFP = recurrence-free progression (reproduced from [1] with permission)
Prostate cancer screening however comes at a price. Although the diagnosis in men who would develop symptomatic prostate cancer later during their life is advanced to a phase in which opportunities for curative treatment are still available, some others are diagnosed with a relatively low risk type of the disease. This low risk prostate cancer would sometimes not have given any symptoms during their life. Overdiagnosis is the main disadvantage of screening. Besides the heavy psychological impact of being diagnosed, many patients receive radical therapy despite the very low risk of progression and some of them can be considered overtreated. Dependent on the therapy chosen (surgery, external or internal radiation), this can potentially lead to erectile dysfunction, incontinence, and bowel problems in men who would not have had any problems of their prostate during their lifetime.

Active surveillance has developed as a potential solution for overtreatment. This strategy entails selecting patients with low risk disease who are unlikely to benefit from radical therapy because their disease has a very favourable natural course. These men are then followed using a fixed protocol to detect biological progression and to correct for initial under staging [4]. Deferral of curative therapy is initiated only when indications for higher risk disease are found or based on patient preference. Active surveillance thus disconnects the direct link between diagnosis and treatment.

Active surveillance is different from watchful waiting. Active surveillance is intended to offer curative treatment when there are signs of disease progression during the strict follow-up and is for relatively healthy men. Watchful waiting offers palliative therapy when the disease has progressed to a symptomatic stage and is usually applied in men not fit for surgery or radiation.

The selection of prostate cancer patients who are likely to have an indolent disease course when remaining untreated is a heavily debated topic. Although adequate risk estimation is generally possible, it is currently impossible to 100% certainly select men with indolent disease. A small chance of including patients who actually harbour a high-risk disease remains. However, the potential delay in treatment resulting from the initial expectant management has not been found to unfavourably impact outcomes.

The most widely applied criteria for eligibility for active surveillance are organ-confined prostate cancer at digital rectal examination, with a PSA <10, a PSA density (PSA divided by prostate volume) <0.2, a low Gleason score of 6 (histological aggressiveness) and a limited number of prostate biopsy cores invaded with cancer (indicating low volume disease).

The recent improvements in imaging of the prostate using MRI and the experience for active surveillance, and applied more often in these cases, although not yet a standard part of the selection process. Also, transperineal template biopsies versus transrectal biopsies are known to reduce the misclassification of prostate cancer and are sometimes applied in active surveillance candidates.

After selection, patients are followed according to a fixed protocol. Besides frequently repeating PSA tests, digital rectal examination and repeat prostate biopsies are performed. As the course of the PSA is not always related to repeat biopsy findings, repeat biopsy is usually done after one year, independent of the PSA values. Again, during follow-up, the role of MRI and template biopsies is still evolving.

The uptake of active surveillance in the recent years has varied by country and region but is generally encouraging. The strategy was reported to be frequently used (35.9% of very low and low-risk men) in Victorian patients [5]. Recent reports show that the number of prostate cancer patients, despite very low risk disease, still receive immediate surgery or radiation therapy is very low and that an initial strategy of expectant management is now almost always elected in these cases. Five years after inclusion for active surveillance, around ½ of patients still have not received active therapy and treatment is thus successfully avoided. After 10 years, around ¼ are still on active surveillance. There are no indications for an unfavourable impact on oncological outcomes. The psychological impact of active surveillance seems also to be limited. However, it should be noted that a selection bias is present in which only the patients who are keen on delaying treatment and avoiding side effects do actually choose active surveillance [8].

Active surveillance has so far been a successful strategy to delay or avoid the side effects of active treatment in patients who would not have any symptoms of their disease if they had never been diagnosed at all. The strategy largely covers the main side effect of screening, which will continue to happen, either as opportunistic screening in individuals or as population based screening. As the risk estimation of diagnosed prostate tumours improves, the indication for active surveillance will decrease as well. MRI and serum biomarkers are the topic of many research efforts currently and will be incorporated to improve active surveillance protocols. At the same time, the psychological and physical burden for patients diagnosed with a low risk prostate cancer needs to be kept as low as possible. The future will both improve the selection process with lower misclassification rates of active surveillance candidates, but also expand the eligibility for active surveillance, for example in older patients. Not treating prostate cancer has never been so important.

References
Intermittent therapy - Intermittent therapy for men with biochemical failure has been shown to be inferior to continuous lifelong therapy [19], and is warranted in most patients. This approach, first reported in 1986, has proven to be effective when properly selected patients, strictly following maintenance of T castration level and switching to intermittent therapy when indicated [20-22]. Currently, it offers improved quality of life in selected patients to testosterone recovery during off-treatment periods. However, some principals should be followed [23]. Only drugs leading to castration should be considered, the initial cycle must last between 6 and 9 mo, and the treatment is stopped if PSA levels have a clear PSA response, empirically defined as a PSA level <4 ng/ml in metastatic patients or <0.5 ng/ml in relapsing patients. The treatment is continued until there is either clinical progression or the PSA value rises above an empirically fixed threshold. Treatment is continued as in the inductive cycle or until PSA reaches nadir. A strict follow-up is mandatory. In the context of radiotherapy, androgen deprivation therapy (ADT) was proven to have biochemical and clinical progression benefit, yet an overall survival benefit has not been demonstrated [19, 24, 25]. In men with more advanced disease, immediate ADT therapy is a common practice. The Eastern Cooperative Oncology Group (ECOG) 3886 trial influenced clinical practice by showing improved OS and CSS in node positive disease patients after RP who were started on ADT immediately upon diagnosis, achieving improved metastasis-free survival, including the use of intermittent ADT in men with node positive disease, or delaying ADT until PSA failure (rather than metastatic disease), have never been studied in a prospective randomized trial. Both approaches are widely used. Patients with metastatic PCa experience reduced risk of complications and a survival benefit with immediate ADT initiation [27]. As a consequence of the adverse effects of ADT on metabolism and quality of life, an intermittent therapy approach has gained popularity.

Given the known adverse effects of ADT, routine follow up is important. Patients should be evaluated at least 3 and 6 months after the initiation of treatment, including serum PSA measurement, DRE, serum testosterone, and evaluation of response and side effects. ADT should be tailored for individual patient based on comorbidities, including the number of cardiovascular risk factors, and the treatment given, usually every 3-6 months. The testosterone serum level should be monitored closely to ensure adequate testosterone suppression. If IAD therapy was chosen, testosterone should be monitored during the off-treatment interval [23]. Routine monitoring of weight, blood glucose, diabetes re-education and blood lipids should be performed on a regular basis. Suggested interventions to reduce adverse effects impact is summarized in table 1.

In conclusion, Androgen ablation therapy is an effective treatment for patients with advanced prostate cancer. Although not curative on its own, it improves survival. It enhances the effectiveness of radiation treatment. The adverse impact on quality-of-life should be taken into consideration, particularly when ADT is used over a long period of time. Intermittent therapy may reduce this OIP impact. Treatment should be tailored to the patient, who should be monitored routinely for response, adverse effects and disease progression.

References
Androgen deprivation therapy: what is the role of the general practitioner? 

Dr Jane Crowe  
Ms Helen Crowe  
General Practitioner  
Urology Nurse Practitioner  
Epworth Prostate Centre  
Epworth Prostate Centre

Androgen deprivation therapy (ADT) by way of chemical or surgical castration still plays an integral part in the management of prostate cancer [1]. ADT is generally used as a treatment option for patients with metastatic prostate cancer [2]. It is also often used as neoadjuvant/adjuvant therapy in combination with radiotherapy for treatment of localized disease [3].

ADT may be given as a continuous therapy, usually 3, 4 or 6 monthly injections, or may be intermittent, with the ADT being commenced and continued for a prescribed time (often 9-12 months) then ceased. The patient’s PSA is monitored regularly and used as a trigger for the recommencement of ADT. Intermittent therapy may allow patients relief from the troublesome side effects by recovery of testosterone. There is conflicting evidence about the optimal use of ADT, and the risks and benefits of continuous versus intermittent therapy [4-6]. Most patients will progress to develop a resistance to their ADT, known as castrate resistant disease, evidenced by a rising prostate specific antigen (PSA) or radiographic evidence of disease progression in the context of castrate levels of testosterone [1]. The time to castrate resistance varies considerably. These patients will then require additional therapies to control their disease.

ADT can result in physical (cardiovascular), psychological, metabolic and bone effects (Table 1), which vary in severity from being mild to intolerable for some patients. The GP needs to be aware of these side effects so they can play a role in monitoring and support of men on ADT as part of a multidisciplinary team.

This therapy is usually commenced by the patient’s treating specialist, with follow up care given by the GP to actively supervise the patient’s side effects. In practice unfortunately, many GPs are unaware of the monitoring practices required for patients on ADT.

GP Management:

The patient, and importantly their partner, require education about ADT and its role in prostate cancer treatment. It is helpful to talk to men and their partners about ADT and to discuss the possible side effects, management, and the optimal follow up program before commencement of therapy. The commonly experienced side effects of ADT, and possible management of these, are listed in Table 1.

A typical clinical assessment and consultation for a patient on ADT would include the following:

1. General assessment.
   - Prostate cancer history
   - Medical history
   - Psychosocial history
2. Investigations.
   - Circumference, blood pressure.
   - General physical examination including height
3. Cognition / mood and depression
   - Psychological (or psychiatric) referral for patient and/or partner antidepressants.
   - Exercise prescription may help with depression and fatigue [12, 13]
   - May require cessation of ADT if depression is severe enough.
   - Memory aids e.g. lists, appointments diaries to help forgetfulness
4. Bowel symptoms
   - Monitoring BMI, blood pressure and fasting lipids.
   - Tight control of CVS risk factors (BP aim for <130/80) [17]
5. Sexual dysfunction
   - Aromatase inhibitors and short term tamoxifen may reduce the pain [14]
6. Gynaecomastia
   - May require cessation of ADT if depression is severe enough.
   - Exercise prescription may help with depression and fatigue [12, 13]
7. Cardiologist
   - Regular check of cardiovascular risk factors (BP aim for <130/80)
   - Lifestyle measures: healthy weight, smoking cessation, exercise
8. Endocrinologist
   - Hormonal treatment: with oestrogen and cyproterone can be effective but have a side effect of significant increased cardiovascular risk, and are not commonly used [14]
9. Urologist
   - Anda prostate nurse
10. Psychologist
   - Referral to a sex therapist
11. Urology/prostate cancer nurse
   - Cognitive behavioral therapy and exercise classes
12. Gynaecologist
   - Aromatase inhibitors and short term tamoxifen may reduce the pain [14]
13. Radiation oncologist
   - Radiation may reduce breast tenderness [14]
14. Referral to a continence physiotherapist
15. GP Management:
   - Periodic follow up
   - Regular PSA monitoring
   - Regular check of cardiovascular risk factors
   - Nutritional assessment
   - Risk of osteoporosis
   - Pain, and other symptoms
   - Early recognition and management of side effects
   - Early referral to specialist services

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In summary, men on ADT for prostate cancer may develop significant side effects. A GP, who is proactive regarding patient education, and in monitoring and managing side effects as part of a multidisciplinary team, can start to improve the health and quality of life of these patients and their partners.

References
Nursing support for men with prostate cancer

Evie Mertens
Department of Urology, The Royal Melbourne Hospital

Urology Nurses are integral members of the multidisciplinary team. They are highly specialized, often with postgraduate qualifications specific to prostate cancer and Urology and Continence nursing. Those specializing in prostate cancer play a pivotal role in providing ongoing education and supportive care to patients and partners with prostate cancer, from diagnosis through to treatment and follow up.

Nurses are often excellent communicators, and developing rapport with the patient and partner from the first consultation is particularly important, as personal topics are broached regarding sexual function and continence. Patients may share information with their nurse that they withhold from the medical team, finding it too embarrassing to discuss certain health care needs or concerns.

A recent survey of 1001 men across 7 countries highlighted this issue, finding “83% of men living with prostate cancer had unmet supportive care needs” [1]. Of those men surveyed, lack of advice from a nurse or advice and support from a nurse and partner were associated with unmet psychological, sexual and health information needs [1]. This survey highlights the significance of the urology nurse addressing the educational and supportive requirements of prostate cancer patients.

Receiving a cancer diagnosis can be a traumatic experience for both the patient and their partner. Historically patients were given their diagnosis and received treatment without adequate education or involvement in the treatment decision. Patients often felt hurried, unable to ask questions about their own health care. Utilising a urology nurse specializing in prostate cancer care enables the patient and partner to receive education using laymen’s terms regarding diagnosis, treatment options, side effects of treatment, and follow up. Deciding on treatment can be extremely stressful for patients and partners; treatment regret can have a huge impact on quality of life, and reducing treatment regret may improve mental health [2]. The prostate cancer urology nurse can ensure patients are seen by both a radiation oncologist and urologist to discuss treatment options, and can provide education and unbiased information regarding surgery or radiotherapy and the side effects of treatment. Linking patients in with their closest prostate cancer support group, and other members of the multidisciplinary team including psychologists and continence physiotherapists ensures the patient receives the best care possible.

At the Prostate Cancer Centre in Melbourne, several specialist clinics are now available to assist men living with prostate cancer. Those patients undergoing Robotic Radical Prostatectomy are enrolled in our Prehabilitation clinic: a multidisciplinary clinic with a urology nurse, continence physiotherapist and exercise physiologist. During a one-hour consultation with the urology nurse the patient and partner are educated on Gleason score, anatomy and function of the urinary tract, surgical procedure, ward stay, incontinence ailes, erectile dysfunction, incontinence and penile rehabilitation. The continence physiotherapist then educates the patient on pelvic floor exercises and the exercise physiotherapist prescribes an exercise regime. Sexual function can be an ongoing issue following curative treatment. A sexual function nurse led clinic runs fortnightly at the Centre with consultant support. The urology nurse is able to educate patients on penile rehabilitation, PDE5 inhibitors, vacuum erection devices and provide lessons in intracavernosal injection therapy. For those patients with advanced disease on androgen deprivation therapy (ADT), there is an ADT clinic where the patient is seen by a GP, urology nurse and exercise physiologist. The urology nurse provides education on the role of testosterone in the body, hormone treatment, side effects of hormone treatment and management of side effects. The GP conducts a comprehensive health check and the exercise physiotherapist prescribes an exercise regime to combat the side effects of hormone treatment.

While service delivery and roles vary between institutions, urology nurses caring for men and partners with prostate cancer share a common goal: to improve patient outcomes through education, support and care facilitation. They are the patient advocate and work hard within the multidisciplinary team to ensure the patient and their partner receives the best outcome. In 2012, the Prostate Cancer Foundation of Australia, funded by Movember, launched a specialist prostate cancer program. Thirteen nurses with prostate cancer care training were rolled out to metropolitan and remote communities throughout Australia, to play a direct role in providing prostate cancer supportive care to patients and family members with prostate cancer. The successful program has now expanded to include twenty-six specialist nurses. Together with urology nurses working in a similar role, Australian men now have improved access to specialist nurses to help meet their ongoing supportive care needs.

References

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Understanding urinary incontinence after radical prostatectomy

Dr Fairleigh Reeves
Departments of Urology and Surgery, Royal Melbourne Hospital, University of Melbourne

Normal anatomy of male urinary continence

In order to understand both the pathophysiology and treatment of incontinence after surgery, it is important to first appreciate the normal anatomy.

Male urinary continence requires the coordinated function of several sets of muscles. Foremost is the male urethral sphincter. This comprises an internal smooth muscle sphincter (also known as the lissosphincter) and the striated external urethral sphincter (also known as the rhabdosphincter) [1].

The lissosphincter is important for continence at rest and also prevents retrograde ejaculation. It receives autonomic innervation.

In contrast, the rhabdosphincter is important for maintenance of continence in conditions of stress. It is weakness of this muscle that is most often implicated post-prostatectomy urinary incontinence. The rhabdosphincter is a horseshoe or omega shaped muscle [2], which has the bulk of its muscle at the anterolateral aspect of the membranous urethra, and inserts posteriorly into the perineal body. Its muscle fibres however also extend proximally, where they thin out over the bladder base and intermingle with the smooth muscle fibres of the bladder [1, 3].

While the rhabdosphincter lies in close proximity to the muscles of the pelvic floor they are in fact independent, separated by connective tissue [4].

The muscular pelvic floor, formed by levator ani also plays an important role in the maintenance of continence [5]. Of particular importance, the most central portion of levator ani consists of specialized thickened muscular slings, which are anchored to the pubic bone anteriorly and pass around the viscera of the pelvis. These muscular slings include puborectalis [5] and puboperineales (also known as levator urethrae or levator prostate [6]).

Functional imaging with transperineal ultrasound has greatly improved our understanding of the coordinated actions of the muscles of continence. Figure 1, illustrates the complementary movement generated by activation of these muscles in men. By measuring the displacement of anatomical points with transperineal ultrasound, Stafford and colleagues were able to demonstrate the various actions of these muscles. That is, the striated urethral sphincter compresses the urethra in a dorso-ventral direction, against the perineal body. Whereas the puborectalis muscle of levator ani displaces the urethra in the opposite direction, anterosuperiorly [7]. Similarly, based on 3D images constructed from MRI, Myers and colleagues suggest that puboperineales achieves quick stop urinary control by compressing the urethra anteriorly against the pubic bone [5].

Why does incontinence occur after radical prostatectomy?

Although urodynamics studies have shown that weakness of the rhabdosphincter is implicated in the majority of cases [9], the precise mechanism underlying this sphincter weakness is not well understood and is likely multifactorial.

Who is most at risk?

A number of factors have been associated with continence outcomes. Older patient age has been associated with poorer continence outcomes [10]. However, in a local series published by Basto and colleagues, there was no significant difference between continence rates at 12 months in men younger than 70 years old compared to those 70 or older. Therefore, age should not be a reason to deny older men with reasonable life expectancy curative surgical treatment of localized prostate cancer [11]. Urinary continence outcomes are also affected by the presence of prior radiotherapy. Salvage radical prostatectomy (following prior radiotherapy) is generally associated with a higher risk of incontinence than primary surgery. Conversely, rates of postoperative and late urinary complications following radical prostatectomy are significantly reduced if the procedure is performed in a high-volume centre and by a surgeon who performs a high number of procedures [12]. Other patient factors that were identified in a meta-analysis, include body mass index, comorbidity index, lower urinary tract symptoms and prostate volume [10]. However, these are not consistently reported.

Despite, various advancements in surgical technique, we have not yet been able to eliminate the risk of post-prostatectomy incontinence. More research is needed to elucidate the precise anatomy of urinary continence so that we can tailor treatment to avoid incontinence.

What can clinicians do?

The most important thing that clinicians can do is to be proactive in the management of urinary incontinence. Unfortunately, we can be a poor judge of our patients’ symptoms. Studies have shown that physician ratings of patient symptoms do not correlate well with patient self-assessments of health related quality of life and are likely to underestimate patient symptoms [13]. This reminds us that we must always actively ask our patients about their continence status so that we can facilitate early intervention and referral to appropriate clinicians for further evaluation and treatment.

A broad spectrum of effective interventions are available to these patients, further details of which are encompassed in the articles by Dr Born, Ms Morrison and Ms Heasly in this edition of The MANual.
Urinary incontinence is a common problem for men after surgery for prostate cancer [1], and it can have a huge impact on quality of life. Pelvic floor muscle training is an essential component of a conservative management program for post-prostatectomy incontinence. A Cochrane review published in 2015 reported moderate evidence that pelvic floor muscle training commenced prior to radical prostatectomy is effective in hastening recovery of continence [2].

Urinary incontinence after radical prostatectomy can be a mild problem, needing pads to manage it for only a few weeks, or more severe and requiring protective pads for up to a year. This leakage will often happen with sudden movements, physical activity, or coughing and sneezing. How much urine leaks and how long this incontinence lasts is difficult to predict. Fortunately, urine leakage can be reduced by learning to use the pelvic floor muscles effectively. The pelvic floor muscles control the bladder and flow of urine. Exercising them effectively will help men regain bladder control earlier after surgery. Ideally the exercises are started before surgery, but they can also help bladder control if they are started after surgery.

What causes post-prostatectomy incontinence?

Aetiology of post-prostatectomy incontinence is complex. The most well recognised cause of post-prostatectomy incontinence is intrinsic sphincter deficiency or weakness. However, there is poor understanding and awareness about the contribution of bladder overactivity, as much of the literature is focused on sphincteric weakness. Bladder overactivity can be pre-existing, or it can be novo after surgery. De novo bladder overactivity is believed to be caused by partial decentralisation of the bladder during or after surgery, or by urine escaping into the proximal urethra due to sphincteric weakness, which can then trigger a bladder contraction [3, 4]. Bladder overactivity is relatively common after radical prostatectomy, occurring in 11-82% of men, however it is rarely the sole cause of post-prostatectomy incontinence [4]. Current research suggests that the aetiology of post-prostatectomy incontinence is multifactorial, and so management must include a thorough history, and an individualised treatment approach.

How can a pelvic floor physiotherapist help?

Pelvic floor physiotherapists specialise in the assessment and treatment of post-prostatectomy incontinence. A thorough subjective assessment, preferably performed pre-operatively ensures identification of pelvic floor muscle risk factors and pre-existing lower urinary tract or bowel symptoms that may impact on post-operative recovery. Understanding each man’s lifestyle and general exercise habits also assists in setting realistic post-operative goals. Establishing baseline outcome measures ensures appropriate post-operative expectations with respect to function and time frames. These measures include bladder frequency volume and fluid intake charts.

It is essential that men have an individualised objective assessment of their pelvic floor muscles with a pelvic floor physiotherapist, to ensure they have the correct technique of activation. The pelvic floor can be effectively assessed via a digital rectal examination, or via transperineal ultrasound. Transperineal ultrasound is a new and exciting assessment technique that has many advantages. It is relatively novel in assessment of the male pelvic floor, although it has been used in female pelvic floor muscle dysfunction for the past 10 years. It has proven an exciting assessment technique that has many advantages. It is relatively novel in assessment of the male pelvic floor, although it has been used in female pelvic floor muscle dysfunction for the past 10 years. It has proven to include functional pelvic floor exercises. Techniques to assess the pelvic floor have also progressed, with the use of transperineal ultrasound emerging in research and practice.

In the past, there was controversy about the efficacy of pelvic floor exercises in the treatment of post-prostatectomy incontinence, with some studies finding it beneficial, and some finding it not beneficial [7]. One key factor that needs to be critically analysed is the way that pelvic floor muscle exercises are taught. A common feature in studies finding no benefit of pelvic floor muscle training is a focus on anal sphincter activation, for example using verbal cues such as ‘tighten around the anus’, or the intensive use of anal biofeedback [8-10]. Conversely, studies that found pelvic floor muscle training effective, had minimal or no emphasis on the anal sphincter [11-13]. In an Australian study in 2015, Stafford and co-authors found that verbal cues with an anal focus create higher external anal sphincter activity, and verbal cues focusing on shortening the penis or flow stopping create the highest urethral pressure, hence being the most preferred [14]. It is likely that pelvic floor muscle training programs focusing on activation of the levator ani and urethral sphincter, rather than the anal sphincter, will continue to see a further improvement in the recovery rate of continence and degree of incontinence after surgery.

References

Evaluation and management of incontinence after treatment for prostate cancer

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The treatment options for localized prostate cancer have been expanding over the past decade. Newer treatments have not been shown to improve cancer control; however, there is some evidence of fewer side effects for the common complications of urinary incontinence and/or erectile dysfunction. These treatments include robotic prostatectomy, whole-gland and focal cryotherapy, high-intensity focused ultrasound and focal laser therapy as well as several types of experimental focal therapy. However, despite improvements in outcomes and a slow migration towards centralization of care, post-treatment incontinence remains a problem for a significant number of men.

Any examination into post-treatment incontinence must begin with the realization that not all men are continent prior to treatment. Men with large prostates and bladder outlet obstruction can suffer from post-void dribbling; in addition, overactive bladder can cause urge incontinence. In a U.S. national sample of men above age 50, 6.4% reported incontinence, but this number increased with age >70, BMI >30 and was significantly higher (21%) in men with moderate or severe depression [1].

Radical prostatectomy can improve some of the lower urinary tract symptoms associated with an enlarged prostate while radiation may ameliorate these symptoms. In the long term, radical prostatectomy is associated with a higher risk of urinary incontinence than radiation, but both of these treatments can cause incontinence. This has been attributed to urethral sphincter injury and to bladder dysfunction, for example detrusor overactivity or poor compliance.

One recent trial in Sweden evaluated 2431 men who underwent either robotic prostatectomy or open radical retropubic prostatectomy [2]. This was a prospective, controlled but non-randomized comparison trial. At 12 months, approximately 20% of men in each group had urinary incontinence as measured by needing to change pads at least once in 24 hours. About 6% of men had moderate incontinence—2-3 pads/day. Severe incontinence, >3 pads/day, was rarely reported by only 2-3% of patients. Of interest, however, was that while the primary end-point of incontinence was measured as the pad-free rate, 35% of men in each group reported daytime leakage, and >3 pads/day, was rarely reported by only 2-3% of patients. Of interest, however, was that while the primary end-point of incontinence was measured as the pad-free rate, 35% of men in each group reported daytime leakage, and about 56% of men experienced incontinence as defined as neither leak-free nor pad-free.

Evaluation of patients with post-treatment incontinence focuses on elucidating the severity of incontinence as well as potentially reversible causes. Primary evaluation is made up of: patient history, physical examination, urinalysis, postvoid residual, voiding diary, and pad test [3]. More specialized examination, such as cistourethroscopy and urodynamics may be required if conservative measures fail [4].

There are several treatment options for addressing post-treatment incontinence which are based on the severity of the incontinence. For mild incontinence, noninvasive therapeutic strategies include conservative treatment, Kegel exercises with or without biofeedback, penile clamp and medication. Surgical intervention includes collagen injection, sling, or artificial urinary sphincter. [Figure 1]

Non-invasive Therapy

A recent randomized controlled trial of patient-centered interventions randomized 279 patients to 3 groups: 1) Biofeedback pelvic floor muscle exercise (PFME) plus a support group; 2) Biofeedback PFME plus telephone contact; 3) Usual care [5]. Both biofeedback groups had a lower frequency of daily urinary leakage than the usual care group at 3 months but not at 6 months. Overall both biofeedback groups reported less symptom severity (p ≤0.001) and fewer incontinence issues (p ≤0.01) than the usual care group at 6 months. For patients with overactive bladder, either demonstrated by urodynamics or suggested by symptoms, antimuscarinic pharmacologic therapy may be beneficial [6].

Surgical Therapy

Because incontinence generally improves over the first 6-12 months after treatment, surgical intervention is generally not indicated for at least a year after prostate cancer treatment [8]. The mainstay of surgical therapy is the male sling and the artificial urinary sphincter. Collagen injections do not seem to deliver long-term efficacy and have largely been abandoned.

The degree of preoperative incontinence affects cure rates in sling surgery. Higher success rates for slings are seen for men with 24h pad weight < 400g which translates into 2 or fewer pads used in 24 hours [7]. The gold standard for post-prostatectomy incontinence surgery is the artificial urinary sphincter. Most studies demonstrate overall success rates > 80% which is variably defined as pad use of 0-1 pads/day or a 50% improvement in pad usage [8]. Mean infection and erosion rates are about 8.5% while device failure ranges from 2-14%. Overall, this translates into a 26% reoperation rate [9].

New Directions

As more patients survive and thrive after cancer treatment, a greater emphasis on survivorship is emerging. The ProRehab study sought to evaluate the effects of a multimodal exercise program on physical fitness, quality of life and treatment-related adverse effects in patients following radical prostatectomy [10]. The trial involved a 15 month supervised exercise program post-prostatectomy of 60 min/week of aerobic, resistance and pelvic floor exercises as well as games and exercises that promote flexibility, coordination, relaxation skills, cognitive abilities, cooperation, and communication. There were no differences between the intervention and control groups in recovery of erectile function or physical activity levels. However, while both groups showed improvement over time in urinary function, there was a significant difference in the urinary symptom score (p = 0.027) favouring the intervention group. Finally, and perhaps of most importance, there were significant intervention-related improvements in physical fitness, urinary incontinence, physical, emotional, and social functioning, as well as further disease and treatment related side effects (dyspea, urinary, and bowel symptoms) compared to the control group.

References

Suicide risk after a prostate cancer diagnosis

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Introduction

Australian men diagnosed with prostate cancer face a higher risk of suicide than their prostate cancer free peers. A recent Cancer Council NSW study found a 70% higher risk in prostate cancer patients. Those at greatest risk were men with locally advanced disease, single men and those living in major cities. Acknowledging this risk exists, instigating a system for early identification of vulnerable men and then implementing referral to appropriate services or programs can reduce the heavy burden that suicide has on this group of men.

Background

Suicide is estimated to account for over 600,000 deaths annually worldwide [1]. While the trend in rates in Australia has fluctuated since records were first kept in 1920, suicide currently accounts for about 2,500 deaths annually, making it the 14th leading cause of death in Australia. A critical period shortly after diagnosis has been identified, with men at over 8 times as high risk of suicide compared to cancer free men within one-week of diagnosis [6]. A recent study demonstrated that risk was not only high in men with high-risk disease, but also in men with low-risk disease within the first six months of diagnosis [7]. Analyses of the USA SEER data has shown patients who were recommended treatment but did not receive it or refused it had a 32% higher risk of suicide than men with other cancers [8].

Clinical depression associated with a cancer diagnosis, distress associated with difficult treatment decisions, or longer-term treatment-related adverse effects such as urinary incontinence and erectile dysfunction that impair quality of life may contribute to heightened risks during the disease course. Prostate cancer patients can experience negative intrusive thoughts and significant declines in physical, mental, and social aspects of their lives, particularly within the first six months of diagnosis. In a large Australian population based study 54% of men with prostate cancer expressed some level of unmet psychological need, and one in five men had moderate to high unmet need for support about uncertainty about the future [9].

Recent Cancer Council NSW Research

With this background it is therefore little surprise that a recent population-wide linkage study in New South Wales identified that men diagnosed with prostate cancer were at a 70% higher risk of death from suicide than age-matched men from the general population [10]. The study was based on 52,000 NSW men diagnosed with prostate cancer between 1997 and 2007. A total of 49 suicides were observed in the patient population. The highest risk occurred in men with locally advanced disease, men living in major cities and those who were single, divorced, separated or widowed. The majority of suicides occurred within six months of diagnosis. Data on the existence of pre-existing psychological or psychiatric illness were not available. Evidence that men are more likely to experience neuro-cognitive and mood function changes, depression, lack of energy and reduced vigour when treated with androgen deprivation therapy may account for some of the higher risk in men with locally advanced disease.

International Evidence Of Higher Risks

Suicide rates are higher in patients previously diagnosed with cancer than in the general population. Lung, oropharyngeal, breast and pancreatic cancers have previously been associated with high rates of suicide internationally [3]. Western Australian cancer patients were shown to have a 60% higher risk of suicide after diagnosis compared to matched population rates [4]. The long term risks of suicide after a diagnosis of prostate cancer varied from between about 4 times higher in men from Florida [5] to 2.6 times higher in Swedish men [6].

Having visited a physician one month prior to death and a recent diagnosis of depression have both been found to raise risk of suicide in men with prostate cancer [5].

What Should Be Done?

Although the absolute risks of suicide in Australian men with prostate cancer are modest, in relative terms the increased relative risk is alarming. Every suicide leaves a trail of destruction in its wake. Not only for families and friends but also emergency services workers and the health professionals who provide care and support for those affected. Our findings reflect only the tip of the iceberg in the spectrum of psychological stress that men with prostate cancer experience after diagnosis.

How we identify these vulnerable men and provide them with a practical toolkit of measures to reduce this risk is of high priority. Identification of those at risk as early as possible in the diagnostic pathway to ensure assessment and appropriate referral to psychosocial care should be an integral part of the patients care plan [11] and indeed has been accepted as a standard of care internationally [12]. The use of a brief, simple, no cost, Distress Thermometer has been recommended with a prostate cancer specific version well validated in men with prostate cancer [13] and available from the Prostate Cancer Foundation of Australia. (http://www.prostate.org.au/media/458256/Prostate_Cancer_Distress_Form.pdf)

If anxiety, distress or depression are suspected or identified, a number of interventions can be activated depending on the needs of the man. These can include referral to appropriate care, peer support, exercise programs or group-based interventions [14].

Conclusion

No man with prostate cancer should suffer alone. The most severe outcome associated with the distress of diagnosis or treatment is arguably suicide. Reducing the risk of suicide after diagnosed with prostate cancer is challenging but a systematic approach to identification and tailoring interventions to an individual can and will make a difference.

References

Online patient wellbeing programs and their families

Comprehensive wellbeing programs online are growing but very few exist that have been specifically designed for prostate cancer. www.MyRoadAhead.org is an online psychological intervention that we have been evaluating as part of our research program and we have found some very promising results. This 6-module psychological intervention is designed to support men in processing the emotional, physical and relationship impact of localized prostate cancer. Our research results indicate that this program significantly improved men's mood, their sexual satisfaction and their masculine self-esteem.

We've also developed an online psychological intervention for partners of men with prostate cancer who would like to reduce their stress, understand prostate cancer and the impact it can have on themselves and their partner and enhance their relationship and communication: www.partners.prostate.org.au

Dr Leslie Schover from MD Anderson in the US has developed online counseling program for men with sexual difficulties following cancer. This program provides expert information, self-help tools and ways for partners to get involved too. www.hardtimessexandcancer.com

www.rekindleonline.org.au is another program that is currently undergoing research evaluation. Rekindle is a private, personalised online resource that addresses sexual concerns for all adults affected by cancer and while it was not specifically developed for prostate cancer it could offer some very important support to men experiencing significant sexual difficulties after prostate cancer treatment.

Mindfulness meditation has also been shown to be an effective intervention for men with prostate cancer, and it's also a very useful for practice for clinicians to use as well. However, finding someone to teach you mindfulness meditation can sometimes be difficult and as a result many people are turning to technology to learn how to practice Mindfulness. www.SmilingMind.com.au offers a free mindfulness App that offers mindfulness meditation programs for people of any age and is a great tool to help you get started with Mindfulness.

Online resources for clinicians

While there are many association guidelines available online (EAU, AUA, NCCN etc) there are also some new and very interesting online resources that are designed to improve the care we as clinicians provide to our patients.

A group of urologists and other clinicians have also started using twitter for an international journal club. It’s an asynchronous chat over 48hrs on the first Sunday/Monday of the month. Use the hashtag #urojc for discussions and follow #urojc to get involved. With almost 4,000 followers it’s a good opportunity to discuss the latest papers with the experts across the world.
Management of lower urinary tract symptoms
caused by benign prostatic hyperplasia

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Lower urinary tract symptoms (LUTS) caused by benign prostatic hyperplasia (BPH) are a common reason for men to seek medical attention. Some men have severe symptoms affecting their quality of life, while others have mild symptoms but seek medical advice fearing that they may be indicative of prostate cancer.

A spectrum of effective medical and surgical management options are available. Men with milder symptoms can frequently be managed with medical therapy, often appropriately initiated in general practice. Alpha-blockers (such as prazosin, alfuzosin, terazosin and tamsulosin) are still first-line therapy and work by relaxing smooth muscle at the bladder neck to reduce bladder outlet resistance. They all work rapidly and have similar efficacy, increasing flow rate by 20-25% and decreasing symptom scores (IPSS) by 30-40% [1]. For those that do not respond, there has been increasing interest in combined medical therapy.

Patients with large prostate glands (>40cm³) and greater than average PSA levels (>1.4ng/ml) may benefit from the addition of a 5 alpha-reductase inhibitor (5-ARI). These agents (such as finasteride or dutasteride) block the conversion of testosterone to dihydrotestosterone and induce apoptosis in prostate epithelial cells leading to a reduction in prostate volume of 18-28% after 6-12 months [2]. In suitable patients this leads to greater efficacy than monotherapy [3], however, at a cost of increased rates of erectile dysfunction and some ongoing concern about an increased incidence of high grade prostate cancer [4]. As such, current prescribing recommendations call for specialist urological assessment prior to commencing 5-ARI therapy.

Recently, Tadalafil, a phosphodiesterase type-5 inhibitor (PDE-5), more commonly prescribed for the treatment of erectile dysfunction, has been shown to improve LUTS, but not flow rates [5]. This effect may be of benefit to those patients suffering from both conditions, but is probably not a cost effective therapy.

For men with more severe symptoms as well as those who cannot tolerate, or would prefer not to have oral therapy, surgery provides a very effective, definitive treatment for LUTS due to BPH. Transurethral resection of the prostate (TURP) remains the gold standard for surgical therapy. A meta-analysis of this widely available and reproducible technique showed a 162% improvement in flow rates and 70% reduction in symptom scores at 5 years [6]. Despite these results, there have been many competing technologies trying to achieve better outcomes.

Laser technologies, such as Greenlight photovaporisation of the prostate (GL-PVP) and Holmium laser enucleation of the prostate (HoLEP) have become increasingly more widely available. Both techniques result in outcomes similar to TURP but with reduced catheterization times and blood loss [7, 8]. Laser technologies are particularly useful in patients on anticoagulation, co-morbidity or with large prostate glands. Their uptake had been limited by the capital cost and skill dissemination, but now these technologies are quite widely available.

Another promising surgical therapy is Prostate Aquablation, an image-guided, robot controlled endoscopic therapy that uses a high-pressure jet of room temperature saline to quickly and accurately resect prostate tissue. Early studies (Phase II) carried out at our institution have been promising showing a 148% improvement in flow rate and 77% reduction in symptom scores at 12 months follow up [9]. All participants were discharged the next day, with patients noting minimal post-operative discomfort. We are currently recruiting patients for a Phase III study randomizing Aquablation to TURP.

Our dedicated LUTS clinic at the APCR Prostate Cancer Centre offers rapid patient assessment with on-site access to flowmetry, ultrasound, urodynamics and flexible cystoscopy, as well as the opportunity for patients to participate in the clinical trials evaluating the latest novel therapies. Referral information can be found at our website www.prostatecentre.org.au.

References