QUALITY OF LIFE RESEARCH IN PROSTATE AND TESTICULAR CANCER

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Abstract

Health related quality of life research is contributing substantially to the management of prostate and testicular cancer, but in different ways. Both diseases have good prognoses, but their trajectories and affected age groups differ greatly. In early stage prostate cancer, there are many different treatment options to choose between and their relative benefits and harms are unclear. Here, health related quality of life research is providing comparative information about functioning, symptoms, wellbeing and preferences to help inform choice. In advanced prostate cancer, the big questions are about whether and when to have various treatments, rather than about the choices between them. Here, health related quality of life research is focused on determining net effects of treatment by measuring benefits in cancer related symptoms, harms from treatment toxicity and allowing these to be considered alongside modest effects on survival. In testicular cancer, the effects of treatment on survival are substantial and options are fewer. Here, health related quality of life research is focused on minimising the effects of disease and treatment on short and long-term health related quality of life by screening, improving supportive care and modifying treatments.

Prostate cancer and quality of life

Prostate cancer accounts for more than 25% of new cancers in Australian men.[1] It typically affects older men and has a relatively slow rate of progression. With increasingly widespread uptake of prostate specific antigen testing, more prostate cancer is being detected at an earlier stage and more younger men are being diagnosed. For younger men, even modest decreases in functioning may have significant impacts on their health related quality of life (HRQoL) over a long period.

Active treatment options for localised prostate cancer include various forms of surgery and radiation therapy, all of which may be associated with significant adverse effects, particularly urinary symptoms and erectile dysfunction. Since high level evidence about the relative survival benefits of these alternative treatments is limited,[2] decisions about treatments need to take account of patient preferences regarding possible trade offs between estimated treatment effectiveness and various adverse effects. While there have been many studies of HRQoL in localised prostate cancer,[3,4] level I evidence for treatment effects on HRQoL has limitations both in methodology and reporting.[5] High quality level II evidence is available from two large cohort studies in the US and Australia, each of which has included a comparison group from the general population.[6,7] At five year and three year follow-up respectively, these studies have found sexual dysfunction to be common in all treatment groups. Urinary dysfunction is reported to be worst in men who have undergone radical prostatectomy. Bowel function is most impacted in those who have received external beam radiotherapy.

Where a cure is not possible, disease management may continue over many years. Men with advanced prostate cancer are typically treated using hormone therapy and then chemotherapy when the cancer becomes hormone resistant. Chemotherapy and/or radiotherapy may also be used to palliate pain from bony metastases. Side-effects associated with hormone therapy include loss of libido, erectile dysfunction, hot flushes, anaemia, obesity, decrease in muscular strength, fatigue, gynaecomastia and breast pain, decline in physical activity and general vitality, mood changes and depression, nausea, diarrhoea and osteoporosis.[8]

HRQoL assessment

Prostate cancer is well served by disease specific HRQoL questionnaires, with at least 10 validated questionnaires available free for use in non-commercial research.[9] Many of these have been developed for localised disease and assess urinary, bowel and sexual functioning. Because men will vary in the importance they attach to the same symptoms and impacts on functioning, it may be important to include items relating to 'bother' as well as severity.[10] This is the approach taken by the widely used EPIC (see glossary), which is an expanded version of the UCLA PCI (see glossary), with additional items assessing impacts from hormone therapy to the core urinary, bowel and sexual domains. The UCLA PCI and EPIC have been used in the two largest studies of HRQoL in localised prostate cancer referred to earlier.[6,7] As the EPIC is the more comprehensive two, it is a good choice of instrument for future studies of HRQoL in localised prostate cancer.

Only one dedicated questionnaire has been developed for assessment of HRQoL in men with advanced prostate cancer. The QOLM-P14 (see glossary) was developed as an accompaniment to the EORTC QLQ-C30 (see glossary) in

a trial comparing the effect of mitoxantone and prednisone versus prednisone alone in men with metastatic prostate cancer. However, it is not an official EORTC questionnaire and has not followed their rigorous development protocol. The QOLM-P14 contains three scales (impact of pain on mobility, pain relief and drowsiness) and two single items (hair loss and change in taste).[11]

A prostate cancer specific utility instrument has also been developed, called the PORPUS (see glossary).[12] This instrument provides a single index for economic analyses that is more responsive to changes over time than are widely used, generic utility scales like the EQ-5D (see glossary) and HUI (see glossary). The MAX-PC[13] (see glossary) has been designed to assess anxiety in men with prostate cancer undergoing treatment and in the survivorship phase. Disease specific assessment of anxiety may be especially important in studies evaluating the impact on HRQoL of watchful waiting.

Because many men with prostate cancer continue to live active lives in the community for many years, it may be appropriate to supplement a prostate cancer specific questionnaire with one assessing generic concerns. The SF-36 (see glossary) and SF-12 (see glossary) are the most widely used generic HRQoL questionnaires both in prostate cancer and across disease groups, and are included in the long and short forms of EPIC respectively. Using the SF-12 or SF-36 enables researchers to compare their results with data from the general population, to identify any general areas of HRQoL that may be significantly lower in the men with prostate cancer in their sample.

Implications for practice

Evidence that men with early stage prostate cancer sometimes regret their treatment decisions after the long-term impacts on functioning become known, supports the need for more detailed discussions between doctors and patients about potential outcomes.[14] Australian research confirms that both clinicians and patients regard the decision making process as complex and difficult.[15,16] A number of decision aids are available but have not been widely used or evaluated in the Australian setting. The large population-based Australian Prostate Cancer Outcomes Study cohort, referred to above,[7] currently provides the best evidence to inform Australian patients and clinicians about treatment choices. The recent publication in the *British Medical Journal*[7] provides three year HRQoL outcomes, using the EPIC, for all active treatment groups plus active surveillance and control groups. Corresponding five year data have been collected but are yet to be analysed, and will be published in due course.

Future research

Further, high-quality randomised comparisons of survival and HRQoL outcomes between treatment modalities for early stage prostate cancer are needed to improve the evidence base for decision making. Studies are especially needed into the impacts on HRQoL of neoadjuvant hormone therapy and new therapies such as cryotherapy. Australian practice would also benefit from the trialling of decision aids for localised disease. In advanced stage disease, research is needed to determine the optimal time for starting chemotherapy.

Testicular cancer and quality of life

Testicular cancer is the most common non-skin cancer in young men, peaking in incidence between the ages of 15 and 45. Since the introduction of cisplatin based polychemotherapy in the late 1970s, testicular cancer has also become one of the most curable of all neoplasms - almost 90% of men affected by testicular cancer can be cured and more than 95% become long-term survivors. While testicular cancer is relatively rare, the young age of the men it affects, the excellent prognosis and a rising incidence (for example, up 25% in Australia from 1993 to 2003[1]) translate into an increasing number of survivors for whom long-term physical, emotional and social wellbeing are major concerns.[17,18]

Early stage testicular cancer is treated by the surgical removal of the affected testis (orchidectomy) followed most often by surveillance, or less often by adjuvant radiation therapy or chemotherapy. Routine retroperitoneal lymph node dissection is rarely used in Australia or New Zealand, but more often in the US. Advanced testicular cancer is most often treated with cisplatin based chemotherapy, sometimes followed by resection of residual disease.

Long-term HRQoL in testicular cancer survivors has not been significantly associated with treatment type,[19] except where the extremes of treatment intensity were compared. Physical and psychosocial dimensions of recovery are often related.

Impacts on physical functioning and health

Cisplatin based chemotherapy is associated with neurotoxic effects such as peripheral sensory neuropathy (parasthesia, pain), which peak about six months after treatment begins; patients are usually able to adapt to the symptoms and they rarely interfere with daily activities.[17] Ototoxicity is a more frequent long-term problem with tinnitus in approximately 25% of patients and perceived long-term hearing loss in 20%. Hearing loss may have an impact on overall health status and ability to work in some survivors.[20] Raynaud's phenomenon, whereby fingers and toes become painful in low temperatures, affects 20% to 30% of men undergoing cisplatin based chemotherapy.

Impacts on sexual functioning may be associated with all modes of treatment, but are worse after radiation therapy and worst after retroperitoneal node dissection.[21] Reductions in sex hormone levels due to chemotherapy, radiotherapy, or surgery can cause decreased sexual function, depression and decreased general physical function.[22,23] Cisplatin based chemotherapy and radiotherapy are also associated with an increased risk of cardiovascular disease and gastrointestinal disease respectively. Mild, though sometimes persistent gastrointestinal symptoms, such as diarrhoea, occur in around a quarter of patients receiving radiotherapy, while more serious problems such as peptic ulcers occur in 3% to 5%. Renal damage from chemotherapy usually remains subclinical, however 30% to 40% of patients may develop hypomagnesemia and hyperuricemia during treatment.[24] Finally, the risk of a second malignancy is significantly higher for testicular cancer survivors than for the general population out to 35 years beyond treatment.[25]

Long-term psychosocial problems

The diagnosis and treatment of a potentially life threatening disease in the prime of life is, unsurprisingly, associated with psychological distress. While the majority of men make a good recovery following treatment, up to a quarter report subsequent problems with psychological wellbeing, relationships, sexuality, body image or employment.[18] These problems often co-exist, but their inter-relationships are not well understood.[26]

HRQoL assessment

EORTC is currently undertaking international validation of a testicular cancer-specific HRQoL questionnaire, the EORTC QLQ-TC26 (see glossary), to supplement its core measure, the QLQ-C30.[27] This study is being conducted in Australia by the Psycho-Oncology Cooperative Group of Australia (PoCoG) in collaboration with the Australian and New Zealand Urogenital and Prostate Cancer Trials Group Ltd (ANZUP).

The QLQ-TC26 assesses treatment side-effects, satisfaction with care, future perspective, job problems, family problems, sexual activity, communication, body image problems, satisfaction with testicular implant, sexual enjoyment and sexual problems. As in prostate cancer, the SF-36 and SF-12 have been used routinely to assess the generic concerns of testicular cancer survivors who have returned to ordinary lives in the community.

Implications for clinical practice

Until recently, the curative potential of treatments for testicular cancer has overshadowed what were perceived to be short-term impacts on HRQoL. However, recent research shows that a minority of men sustain lasting physical and psychosocial impacts in one or more areas of functioning and wellbeing. Given the excellent prognosis for this patient group, the major question is whether HRQoL might be improved by modifying treatments and care pathways without compromising survival. It seems likely that screening might have a role to play in identifying men for whom psychosocial support may be helpful.

Future research

A more detailed profile is needed of men who experience poor outcomes from testicular cancer and its treatment. Outcomes may tend to cluster in predictable ways and some men may even experience pervasive difficulties across many aspects of their lives. Better understanding of the relationships between characteristics of the men, their disease, their treatments and their subsequent problems would inform the design of tailored, multi-disciplinary screening and intervention program to meet the full spectrum of needs. Existing studies have provided piecemeal data that is insufficient to answer these questions. An ongoing intergroup study initiated by PoCoG in collaboration with ANZUP will provide a comprehensive assessment of psychosocial outcomes, disease and treatment variables in a large cross-section of testicular cancer survivors. A subsequent longitudinal study following patients from diagnosis is also planned.

Conclusion

HRQoL research continues to provide important information to assist in the management of men with prostate or testicular cancer. Treatment for the early stages of both diseases typically achieves a cure, but may come at the cost of long-term impacts on functioning and wellbeing. Future research in localised prostate cancer will provide further information about the relative risks to HRQoL of various treatments that will inform decision-making within the context of men's individual preferences. In advanced prostate cancer, the focus will continue to be on the relative benefits and harms of hormone, chemo and supportive therapies for the palliation of metastatic disease. In testicular cancer, research will aim to find ways of limiting the impacts on HRQoL without compromising established benefits to survival.

Glossary

EORTC QLQ-C30	European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire – Core 30
EORTC QLQ-TC26	European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire – Testicular Cancer 26
EPIC	Expanded Prostate Cancer Composite
EQ-5D	EuroQol-5D
HUI	Health Utilities Index
MAX-PC	Memorial Anxiety Scale for Prostate Cancer
PORPUS	Patient Oriented Prostate Utility Scale
QOLM-P14	Quality of Life Module - Prostate 14
SF-36	Medical Outcomes Trust Health Survey Short Form – 36 items
SF-12	Medical Outcomes Trust Health Survey Short Form – 12 items
UCLA PCI	University of California Los Angeles Prostate Cancer Index

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