



Original Article

Primary care follow-up of radical prostatectomy patients: A regional New Zealand experience



Omid Yassaie^{1,2,*}, Ben McLaughlin¹, Marlon Perera³, Todd Manning³, Nathan Lawrentschuk^{3,4,5}, Andrew Malcolm¹

¹ Department of Surgery, Nelson Marlborough District Health Board, Nelson, New Zealand

² Department of Surgery, Capital and Coast District Health Board, Wellington, New Zealand

³ Department of Surgery, Austin Health, University of Melbourne, Australia

⁴ Olivia Newton-John Cancer Research Institute, Melbourne, Australia

⁵ Department of Surgical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia

ARTICLE INFO

Article history:

Received 15 July 2016

Received in revised form

20 July 2016

Accepted 25 July 2016

Available online 29 July 2016

Keywords:

Follow-up

General practitioner

Primary care

Prostate cancer

Prostate specific antigen

Radical prostatectomy

ABSTRACT

Background: Contemporary recommendations regarding the duration of follow-up after radical prostatectomy (RP) are highly heterogeneous. Protocol-based follow-up schemes have been implemented to facilitate the expeditious identification of patients with recurrence. The aim of this study is to assess the reliability and comfort of general practitioners (GPs) in follow-up of RP.

Methods: Following institutional ethical approval, we performed a retrospective review in patients undergoing follow-up after RP between January 2004 and December 2010. Patient factors, disease variables, and follow-up prostate specific antigen (PSA) compliance was collected. “Noncompliant” follow-up care was defined as: patients that had not received a PSA for a 14 month period within 5 years of prostatectomy. Patient and disease-based risk factors for noncompliant follow-up were assessed. GPs were also surveyed in their follow-up practice of RP patients, to assess their familiarity in caring for these patients.

Results: In total, 65 cases were identified that met the inclusion criteria. At 60 months of follow-up, 66% (43/65) of patients had a compliant follow-up regime. For patients with noncompliant follow-up at 60 months, median time of compliance did not differ significantly when assessing preoperative PSA, Gleason sum, extraprostatic extension, or surgical margin status. Of the GPs surveyed, 68% of GPs felt comfortable in follow-up of RP patients. Some 62% of GPs would expect the PSA to be < 0.1 and 25% of GPs would measure the PSA annually.

Conclusion: Our study identified that follow-up by GPs after RP is insufficient. Accordingly, there is a requirement for formal educational programs if primary care is to take a greater role in follow-up of these patients.

Copyright © 2016 Asian Pacific Prostate Society, Published by Elsevier. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Prostate cancer is among the most common malignancy diagnosed in men.¹ Radical prostatectomy (RP) remains as the standard of care for organ-confined prostate cancer and provides excellent oncological outcomes.^{2,3} Following RP, a proportion of patients require additional cancer therapy, such as radiation or hormonal manipulation.⁴ These additional therapies are typically instigated

upon diagnosis of disease recurrence.⁵ At present, prostate specific antigen (PSA) represents the prominent biomarker for disease recurrence following prostate cancer treatment.⁶ Accordingly, the prompt diagnosis of elevated PSA (and likely disease recurrence) is essential as it may effect cancer-specific survival. Prompt diagnosis implies a lesser risk of disseminated disease and may increase treatment options available.

Therefore, it is important to have a robust effective means to follow-up these patients. Contemporary guidelines outlining postprostatectomy follow-up are highly heterogeneous and conflicting. Of these, recommendations range between follow-up periods from 6 months to lifetime. Traditionally, the follow-up has

* Corresponding author. Department of Surgery, Wellington Hospital, 36 Gurkha Crescent, Khandallah, Wellington, New Zealand.

E-mail address: omid.yassaie@gmail.com (O. Yassaie).

been shared between urological and oncological specialists. However, over the past decades, an increasing demand on outpatient clinics has been observed. Additionally, hospital-based follow-up represents a significant source of health care expenditure. These factors have led to the development of nurse-led follow-up clinics. The predominant view of UK health professionals expressed in a qualitative study in 2011 was that there is scope for primary care to occupy a greater role.⁷

To date, there is limited data assessing the reliability and comfort of primary health care physicians with follow-up of prostatectomy patients in the community. We aimed to assess compliance with general practitioner (GP)-based postprostatectomy regimes. We further aimed to identify patient-related risk factors for poor follow-up compliance. Finally, we aimed to assess GPs' understanding of postprostatectomy follow-up.

2. Materials and methods

Following institutional ethical approval, we identified patients that underwent RP between January 2004 and December 2010 by a single surgeon. Patients were excluded if they failed to reach an undetectable PSA postoperatively, experienced biochemical recurrence within 2 years of RP, died within this 2 year time frame, had incomplete documentation, did not have a minimum of 5 years follow-up, or were not discharged to the care of their GP.

The study was performed at Nelson Hospital, Nelson Marlborough, New Zealand. This represents a regional center, consisting of a population of 50,000. Given logistical and accessibility issues, the typical practice of the involved surgeon included a 2 year follow-up after RP. Following this, patient care was transferred to their respective GP for further follow-up. Upon transfer, GPs were advised to perform annual PSA blood tests and refer back to specialist care if there was a detectable PSA or any concerns with complications arising from surgery.

We retrospectively reviewed physical and electronic records. Data collected included: patient demographics (age, comorbidities, ethnicity), prostate cancer (preoperative PSA, final prostate pathology, extraprostatic extension, surgical margin status), and follow-up details (postprostatectomy PSA frequency, follow-up period, presence of biochemical recurrence). To access PSA data, the local laboratory system was accessed and all preoperative and postoperative PSA values were recorded. PSA recordings were categorized in 5 month intervals following prostatectomy.

Biochemical failure after RP was defined as a PSA of 0.2 or higher, as consistent with the current European Association of Urology and American Urological Association recommendations.^{5,8,9} Noncompliant patient follow-up was defined as patients who did not have a post RP PSA reading for 14 months. Duration of compliance was calculated by determining the PSA reading at the longest follow-up interval. Patients that underwent complete PSA assessment to 60 months of follow-up were deemed compliant. This was used as a surrogate marker for reliability of follow-up.

An anonymous electronic online survey (Survey Monkey, Palo Alto, CA, USA) was sent to all of the 118 GPs regularly practicing in

the catchment of the Nelson Hospital health service. This survey was aimed to assess the comfort of GPs in following up RP patients and their understanding of how these patients should be followed up (summarized in Table 1).

Data was entered in an Excel 2013 spreadsheet (Microsoft, Redmond, CA, USA). Analysis was performed using SPSS v20 (SPSS Inc., Chicago, IL, USA). Data was defined as categorical or continuous. Categorical data were analyzed using Fishers' exact test or χ^2 as appropriate. Continuous data were tested for distribution. Parametric continuous data were compared using one-way analysis of variance.

3. Results

In total, 65 patients were identified who met the inclusion criteria. Patient demographics and disease characteristics are highlighted in Table 2. During the study period, overall follow-up compliance was 42% (27/65) following transfer of care to their GP and 58% (28/65) were "noncompliant". However, at 60 months of follow-up, 66% (43/65) of patients had compliant follow-up. During follow-up, five patients were identified as suffering biochemical recurrence. Of these, two cases were not referred back by the GP to the hospital. The remaining three patients were referred back to the urology department and were seen at a median 14 days post-recurrence. These cases represented local recurrence and were referred to radiation oncology for consideration of salvage radiotherapy.

Assessing patient factors as risk for noncompliant follow-up, no factors resulted as statistically significant predictors. Specifically: preprostatectomy PSA > 10 [relative risk (RR) = 0.98, 95% confidence interval (CI): 0.43–2.21], Gleason sum of ≤ 7 (RR 2.6, 95% CI: 0.41–16.3, $P = 0.32$), presence of extraprostatic extension (RR = 0.63, 95% CI: 0.257–1.59, $P = 0.32$), and positive surgical margins (RR = 0.65, 95% CI: 0.23–1.89, $P = 0.43$). For patients with noncompliant follow-up at 60 months, median time of compliance did not differ significantly when assessing preoperative PSA, Gleason sum, extraprostatic extension, or surgical margin status.

In total, 118 GPs were sent the survey and of these, 47 responses were obtained. A majority of GPs self-reported being comfortable in following up with patients after RP. Some 73% of GPs correctly expected a nondetectable or <0.1 PSA value after RP. Conversely, 27% of GPs defined biochemical recurrence at higher levels or were unsure. Table 3 summarizes the results of the survey.

Table 2
Disease parameters for patients.

| Disease parameter | n = 65 |
|---------------------------|--------------|
| Median PSA (ng/mL) | 7.0 |
| Median Gleason grade | 7 |
| Extracapsular extension | 26% (n = 17) |
| +ve margin | 20% (n = 13) |
| Biochemical failure | 8% (n = 5) |
| Median time to recurrence | 43 mo |

PSA, prostate specific antigen.

Table 1
Questionnaire submitted to participating general practitioners.

| Questionnaire |
|---|
| (1) Do you feel comfortable following up patients following radical prostatectomy for prostate cancer? |
| (2) What PSA would you normally expect following a radical prostatectomy for prostate cancer? |
| (3) How frequently would you check PSA in patients following a radical prostatectomy? |
| (4) When would you refer back a patient to urology services following a radical prostatectomy? |
| (5) Would you be prepared to attend education sessions regarding PSA testing following radical prostatectomy? |
| (6) Any other questions or suggestions? |

PSA, prostate specific antigen.

Table 3
Summary of results of survey completed by general practitioners (GPs).

| | |
|---|--------------|
| Do you feel comfortable following up patients following RP for Prostate Cancer? N = 46 | |
| Comfortable | 67% (n = 31) |
| Not comfortable | 33% (n = 15) |
| What PSA would you normally expect following a RP for Prostate Cancer ? n = 47 | |
| Undetectable | 13% (n = 6) |
| < 0.1 | 60% (n = 28) |
| < 1 | 15% (n = 7) |
| < 4 | 2% (n = 1) |
| 10 | 2% (n = 1) |
| Low | 2% (n = 1) |
| Dependent on time postoperation | 2% (n = 1) |
| Unsure | 4% (n = 2) |
| How frequently would you check PSA in patients following a RP? n = 46 | |
| Annually | 28% (n = 13) |
| 6–12 monthly | 39% (n = 18) |
| 3–6 monthly | 15% (n = 7) |
| Guided by Urologist, clinical guidelines, or discharge summary | 11% (n = 5) |
| Not at all | 2% (n = 1) |
| Unsure | 4% (n = 2) |
| When would you refer back a patient to Urology services following a RP? | |
| PSA rise alone | 40% (n = 19) |
| Complications or symptoms of recurrence alone | 6% (n = 3) |
| PSA rise and/or symptomatic of recurrence/complication | 43% (n = 20) |
| As per discharge letter | 2% (n = 1) |
| Any questions | 2% (n = 1) |
| Unsure | 6% (n = 3) |

Of the GP respondents, 83% reported interest in attending educational sessions on follow-up of RP patients. Suggestions from GPs surveyed were as follows:

- Guidelines for PSA monitoring post-RP be made available via the Regional Pathways website
- PSA results for RP patients were not flagged as being post-operative on their laboratory results systems, and thus were viewed and appraised without the appropriate normal range of values
- Clearer instructions on discharge summaries and clinic letters for GPs

4. Discussion

RP remains as a prevalent treatment option in organ-confined prostate cancer. Meticulous follow-up is critical to ensure treatment success and detect disease recurrence promptly. Significant health care economic burden has prompted the introduction of nurse-led and primary care physician-based follow-up regimes postprostatectomy. Limited literature assessing the suitability of GP-based follow-up regimes following RP is available. From our study, we determined that, at present, transfer of follow-up care results in suboptimal postprostatectomy follow-up regimes.

Postprostatectomy follow-up is complex, with multiple critical factors to be assessed. Most importantly, patients may be promptly identified following disease recurrence. Approximately one third of patients suffer from recurrence of disease regardless of treatment modality.^{10,11} In current practice, the PSA serum marker is a simple method of detecting disease recurrence after RP. International guidelines agree on the essential role of routine PSA testing in prostate cancer follow-up.^{8,12} Typically, following prostatectomy, an undetectable PSA level of < 0.2 is expected, in keeping with total eradication of prostate tissue, and thus cure. During follow-up, a detectable PSA suggests biochemical recurrence of prostate cancer and requires prompt assessment, and may require further disease

management. Further, significant advances in molecular imaging have allowed identification of biochemical recurrence at very low PSA levels.¹³ Early identification of disease recurrence prior to metastatic spread allows for a wider repertoire of treatment options. A robust reliable follow-up regime is required in order to identify patients who require further treatment for prostate cancer recurrence. A recent systematic review highlighted the inconsistencies between follow-up recommendations regarding duration and frequency of PSA tests.¹⁴ Of these recommendations, interval between PSA tests in the 1st year following RP varies between 3 months and 12 months. Currently, the New Zealand Best Practice Advocacy Centre guidelines and the UK NICE guidelines are in agreement regarding the recommended frequency of PSA tests following RP. PSA testing should start at 6 weeks at the earliest, with 6 monthly testing for the first 2 years, and then at least annually thereafter.^{7,15–17}

In the current economic climate, there has been a considerable push to reduce the burden of hospital-based services to primary care facilities. In the setting of prostate cancer, nurse-led clinics have been used in several centers in New Zealand, suggesting it is a safe reasonable approach.¹⁸ Current literature supports the involvement of primary health care clinicians in the setting of oncological follow-up. Our survey illustrated that up to 67% of primary health care physicians felt “comfortable” in following up postprostatectomy patients. Of the participating clinicians, over 80% correctly identified PSA testing frequency as annually or more frequently following RP. These findings are in accordance with a recent systemic review, which suggested that a greater GP role in cancer care could improve the quality of patient care for cancer survivors.^{12,19} Lewis et al¹⁹ suggested that hospital follow-up might prompt unnecessary tests, raise anxiety, provide false reassurance, and delay the patient’s return to full function. This systemic review found no difference in patient wellbeing, survival, and recurrence rates between colon and breast cancer patients followed up in primary care compared with those followed up in secondary care, although the follow-up period was limited and studies were not well powered.

Conversely, there is controversy whether primary care based regimes are able to provide an effective follow-up service.²⁰ The findings of the current study highlighted that a significant proportion of patients following prostatectomy received insufficient follow-up when managed by primary health care service-based follow-up regimes. Clinician-based factors may account for a proportion of these patients with noncompliant follow-up. While approximately 70% of primary health care physicians surveyed were aware that following prostatectomy PSA should be undetectable, the remainder incorrectly identified concerning PSA levels. It should be noted that over 80% of the participating practitioners were interested in participating in educational training sessions. These findings are corroborated by Watson et al⁷ who demonstrated that GPs were content to provide a greater role in prostate cancer patients following RP, however they needed greater guidance and support.¹⁷

In our study, we recommended an annual PSA upon discharge to primary healthcare physicians.¹⁵ Despite this, at 5 years follow-up, only 66% of patients had compliant follow-up. These findings are in accordance with previous literature. Goodall et al²¹ recently assessed postprostatectomy follow-up with a strict algorithm-based regime. This group reported compliance of 74% at 24-month follow-up. In addition to clinician-based factors, patient-related factors must be considered when determining causation for noncompliant follow-up postprostatectomy. Intuitively, patients with higher risk disease are more likely to be involved and cooperative with their respective disease management. Despite this, high risk disease characteristics, including high initial PSA,

high Gleason sum, extraprostatic extension, and positive surgical margins, did not infer a reduced risk of noncompliant follow-up. In these patients, meticulous follow-up is critical to ensure acceptable oncological outcomes. Accordingly, discharge of high risk patients for GP follow-up may not be suitable. To date, multiple strategies have been trialed to improve patient compliance. For example, mobile health messaging services have been assessed in alternate domains of medicine.^{22,23} Current literature highlights significant heterogeneity of outcomes, likely a result of varying methodology. A recent Cochrane review outlined some benefit in the compliance of chronic disease.²⁴ Such management may be of benefit in the current assessed model of postprostatectomy follow-up.

There are several limitations of the current study. Firstly, there are inherent limitations with studies of a retrospective nature. Secondly, due to ethical and logistical issues, we were unable to collate data on patients that moved out of the study district. Further, the primary physician cohort included in the current study may not be truly reflective of the practice throughout the remainder of the country. A national study including practices throughout the country may provide more generalizable information. The current study highlights the willingness of primary health care physicians to be involved in prostate cancer management. Finally, data pertaining to a GP's understanding of other pertinent postprostatectomy outcomes were not collected. While this was not the primary aim of the current study, understanding of the importance of urinary incontinence and erectile function is critical in acceptable postprostatectomy follow-up. Formal guidelines in primary care prostate cancer follow-up are required, particularly in the evolving field of prostate cancer management and improved prostate cancer biomarkers.^{6,25}

In conclusion, although most primary health care physicians are comfortable in following up patients following RP, a significant portion of patients are not reliably followed up in this setting. Further education and collaboration between the hospital and primary care may help to align management strategies and follow-up of these patients.

Conflicts of interest

The authors have no conflict of interest.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. *CA Cancer J Clin* 2016;66:7–30.
2. Bill-Axelsson A, Holmberg L, Garmo H, Garmo H, Stark JR, Busch C, et al. Radical prostatectomy or watchful waiting in early prostate cancer. *N Engl J Med* 2014;370:932–42.
3. DellOglio P, Karnes RJ, Joniau S, Spahn M, Gontero P, Tosco L, et al. Very long-term survival patterns of young patients treated with radical prostatectomy for high-risk prostate cancer. *Urol Oncol* 2016;34:234.e13–9.
4. Lu-Yao GL, Potosky AL, Albertsen PC, Wasson JH, Barry MJ, Wennberg JE. Follow-up prostate cancer treatments after radical prostatectomy: a population-based study. *J Nat Cancer Inst* 1996;88:166–73.
5. Heidenreich A, Bastian PJ, Bellmunt J, Bolla M, Joniau S, van der Kwast T, et al. EAU guidelines on prostate cancer. Part II: treatment of advanced, relapsing, and castration-resistant prostate cancer. *Eur Urol* 2014;65:467–79.
6. McGrath S, Christidis D, Perera M, Vela I, Manning T, Lawrentschuk N. Prostate cancer biomarkers: are we hitting the mark? *Prostate Int* 2016;4:130–5.
7. Watson EK, O'Brien R, Campbell C, Weller D, Neal RD, Wilkinson C, et al. Views of health professionals on the role of primary care in the follow-up of men with prostate cancer. *Fam Pract* 2011;28:647–54.
8. PSA testing for the pretreatment staging and posttreatment management: American Urological Association Prostate-Specific Antigen Best Practice Statement Update Panel. [Internet]. [cited 2016 Feb 10]. Available from: <https://www.auanet.org/education/guidelines/prostate-specific-antigen.cfm>.
9. Heidenreich A, Bastian PJ, Bellmunt J, Bolla M, Joniau S, van der Kwast T, et al. EAU guidelines on prostate cancer. Part 1: screening, diagnosis, and local treatment with curative intent-update 2013. *Eur Urol* 2014;65:124–37.
10. Pound CR, Partin AW, Eisenberger MA, Chan DW, Pearson JD, Walsh PC. Natural history of progression after PSA elevation following radical prostatectomy. *JAMA* 1999;281:1591–7.
11. van den Ouden D, Hop WC, Kranse R, Schroder FH. Tumour control according to pathological variables in patients treated by radical prostatectomy for clinically localized carcinoma of the prostate. *Br J Urol* 1997;79:203–11.
12. Meiklejohn JA, Mimery A, Martin JH, Bailie R, Garvey G, Walpole ET, et al. The role of the GP in follow-up cancer care: a systematic literature review. *J Cancer Surviv* 2016. Available from: <http://dx.doi.org/10.1007/s11764-016-0545-4>.
13. Perera M, Papa N, Christidis D, Wetherell D, Hofman MS, Murphy DG, et al. Sensitivity, specificity and predictors of positive 68Ga-PSMA PET: a systematic review and meta-analysis. *Eur J Urol* 2016 [in press].
14. McIntosh HM, Neal RD, Rose P, Watson E, Wilkinson C, Weller D, et al. Follow-up care for men with prostate cancer and the role of primary care: a systematic review of international guidelines. *Br J Cancer* 2009;100:1852–60.
15. Best Practice Advocacy Centre New Zealand. Following up prostate cancer in primary care. [cited 2016 Feb 21]. Available from: <http://www.bpac.org.nz/BT/2012/October/prostate.aspx>.
16. Prostate cancer: diagnosis and treatment. NICE clinical guideline. Available from: guidance.nice.org.uk/cg175.
17. Wilkinson AN, Brundage MD, Siemens R. Approach to primary care follow-up of patients with prostate cancer. *Can Fam Physician* 2008;54:204–10.
18. Anderson B. The benefits to nurse-led telephone follow-up for prostate cancer. *Br J Nurs* 2010;19:1085–90.
19. Lewis RA, Neal RD, Williams NH, France B, Hendry M, Russell D, et al. Follow-up of cancer in primary care versus secondary care: systematic review. *Br J Gen Pract* 2009;59:e234–47.
20. Bulger J, Hiscock J, Neal R. 'Carrying on the way we are is becoming shambolic' – an interview study with prostate cancer specialists about their usual practice of follow-up. *J Clin Urol* 2015;8:240–5.
21. Goodall PP, Little J, Robinson E, Trimble I, Cole OJ, Walton TJ. Initial experience of an algorithm-based protocol for the community follow-up of men with prostate cancer. *BJU Int* 2016.
22. DeKoekkoek T, Given B, Given CW, Ridenour K, Schueller M, Spoelstra SL. mHealth SMS text messaging interventions and to promote medication adherence: an integrative review. *J Clin Nurs* 2015;24:2722–35.
23. Hamine S, Gerth-Guyette E, Faulx D, Green BB, Ginsburg AS. Impact of mHealth chronic disease management on treatment adherence and patient outcomes: a systematic review. *J Med Internet Res* 2015;17:e52.
24. de Jongh T, Gurol-Urganci I, Vodopivec-Jamsek V, Car J, Atun R. Mobile phone messaging for facilitating self-management of long-term illnesses. *Cochrane Database Syst Rev* 2012;12:CD007459.
25. Perera M, Krishnanathan N, Linder U, Lawrentschuk N. An update on focal therapy for prostate cancer. *Nat Urol Rev* 2016;13:641–53.