Original Article

Quality of Radiation Therapy Referral and Utilisation Post-prostatectomy: A Population-based Study of Time Trends

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Abstract

Aims: Adjuvant radiotherapy post-prostatectomy has been shown to benefit patients with adverse pathology. It remains unclear whether salvage radiotherapy confers equivalent outcomes. Practice guidelines recommend referral to radiation oncology within 6 months after prostatectomy to discuss adjuvant and salvage radiotherapy. The study objectives were to assess, at a population level: (i) post-prostatectomy referral patterns for radiotherapy; (ii) adjuvant and salvage radiotherapy utilisation; and (iii) time trends in relation to clinical trials and guidelines. These findings provide indications of access to quality care.

Materials and Methods: This was a retrospective cohort study. Electronic radiotherapy consultation and treatment records were linked to the population-based Ontario Cancer Registry. The population included prostate cancer cases treated with prostatectomy in Ontario between 2003 and 2012. Radiotherapy referral and treatment rates over time were analysed using the chi-squared trend test.

Results: Over the study period, 30 447 prostate cancer patients received prostatectomy. The proportion seen by radiation oncology within 6 months after prostatectomy doubled from 10.7% in 2003–2004 to 21.7% in 2011–2012 (P < 0.0001 for trend), with the largest annual percentage difference in 2009–2011 (3.4%). Among 4641 patients seen within 6 months, adjuvant radiotherapy rates remained at 51.0% ± 3.0%. Contemporaneous with radiation oncology referral trends, overall adjuvant radiotherapy use increased from 6.2% in 2003–2004 to 11.0% in 2011–2012 (P < 0.001), while salvage radiotherapy remained at 8.4% ± 0.4%. Consequently, the total proportion receiving radiotherapy within 24 months increased from 14.1% in 2003–2004 to 17.7% in 2009–2010 (P < 0.0001).

Conclusions: There was an increase in access to early radiation oncology referral post-prostatectomy and adjuvant radiotherapy in Ontario between 2003 and 2012, following guideline publication.

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Key Words: Health care quality, access, and evaluation; prostatic neoplasms; prostatectomy; radiation oncology; radiotherapy, adjuvant

Introduction

The effectiveness of post-radical prostatectomy adjuvant radiotherapy (ART) was reported starting in 2004 in three randomised trials showing a reduction in biochemical relapse in patients with adverse pathology (positive margins, extracapsular extension or seminal vesicle invasion) [1–7]. In 2009, Thompson et al. [8] reported a corresponding survival advantage at 10 years.

Although the state of knowledge describes the benefits of ART, there is ongoing debate as to whether early salvage radiotherapy (SRT) at the time of first detection of prostate-specific antigen (PSA) confers equivalent disease outcomes [9–12]. Early SRT is attractive as about half of patients do not relapse within 5 years, despite having high-risk features [3,4,6]. Randomised trials are underway evaluating the efficacy and timing of SRT versus ART [10,13–16].

On the basis of evolving evidence surrounding ART and SRT, the Genitourinary Radiation Oncologists of Canada (GUROC) published consensus statements in 2008, recommending that consultation with a radiation oncologist early in the postoperative period is advised to discuss benefits and side effects of adjuvant radiotherapy in those with adverse pathological features at prostatectomy.
[17,18]. Similarly, Cancer Care Ontario (CCO) 2008 and 2010 guidelines state that ‘in patients found at radical prostatectomy to have positive surgical margins, extracapsular extension or seminal vesicle invasion, early referral to a radiation oncologist is recommended for consideration of adjuvant external beam radiotherapy with the aim of prolonging survival’ [19]. Early referral implied involving the radiation oncologist in a decision regarding initiating ART 6–18 weeks after radical prostatectomy or identifying patients suitable for follow-up with a view to early SRT.

Despite cumulative evidence and guidelines recommending early referral for radiotherapy after radical prostatectomy, there is a gap in the literature with respect to the impact on rates of early radiation oncology referral after radical prostatectomy at the population level. With advancement of medical knowledge there is a need for the assessment of the effect on care delivery. In an influential framework put forth by the Institute of Medicine, quality of care was defined as ‘the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge’ [20]. Large-scale population-based studies investigating referral patterns after radical prostatectomy are in light of recent evolving evidence are lacking.

The aim of this large population-based study was to investigate the impact of advancement in medical knowledge (including clinical trials and guidelines) on radiation oncology referrals among patients treated with radical prostatectomy in Ontario between 2003 and 2012, to provide an indication of quality of care. A secondary aim was to characterise the extent to which ART and SRT practices have been adopted.

Materials and Methods

Study Design

This was a retrospective cohort study. The study population included all men who underwent radical prostatectomy for prostate cancer in Ontario between 1 January 2003 and 30 November 2012. The study was approved by the Queen’s University research ethics board.

Data Sources and Linkage

Ontario has a population of 13.8 million people, and a publicly funded universal health insurance plan. The provincial cancer agency, CCO, is responsible for coordinating provincial cancer centres, which are the only providers of radiotherapy in Ontario. Radical prostatectomy is carried out in a wider range of public hospitals.

The Ontario Cancer Registry is a population-based registry that collects demographic and clinical characteristics of all patients diagnosed with cancer in Ontario, reported to be >95% complete for all sites combined based on a capture—recapture methodology [21]. Records on incident prostate cancer cases were utilised. Registry data were linked to hospital separation data identifying radical prostatectomy cases (Canadian Institute for Health Information) and to radiotherapy treatment data and radiation oncology visit data (routinely electronically compiled by CCO from each radiotherapy centre).

Radiation oncology visit data from 1 January 2003 to 31 May 2013 were linked to radical prostatectomy cases from 1 January 2003 to 30 November 2012. Radiotherapy records were complete to the end of May 2013, allowing us to report on radiotherapy use within 6 months of radical prostatectomy for cases with index surgery date up to 30 November 2012. Patients treated with palliative intent were excluded.

Definitions of Radiation Oncology Consultation and Radiotherapy Utilisation

The primary outcomes of this study were whether patients were seen by radiation oncology for consideration of ART or SRT and receipt of radiotherapy. We defined early radiation oncology consultation as a first radiation oncology visit within 6 months after radical prostatectomy. All patients who receive a radiation oncology consultation after radical prostatectomy were included in the analysis, regardless of whether they were also seen before radical prostatectomy. ART was defined as curative-intent radiotherapy initiation within 6 months of radical prostatectomy, as previously described [14,22–24]. Sensitivity analyses defining ART as initiation of ART within 4 and 8 months, respectively, were carried out. Curative radiotherapy administered 6–24 months after radical prostatectomy was defined as early SRT. Long-term data are limited by the last date for which we had complete radiotherapy records.

Statistical Methods

Cumulative incidence functions were used to describe cumulative radiation oncology referral and radiotherapy utilisation rates as a function of time since radical prostatectomy. Patients were censored if they did not receive a radiation oncology visit or radiotherapy before 31 May 2013, which was the last date for which we had complete radiotherapy records. Trends in radiation oncology consultation and radiotherapy utilisation over time were statistically tested using the Cochran-Mantel-Haenszel chi-squared trend test. SAS, version 9.4, was used for all statistical analyses.

Results

We identified 30 447 incident cases of prostate cancer treated with radical prostatectomy between 2003 and 2012. The median age at diagnosis was 62 years (interquartile range: 57, 66). The median number of radical prostatectomy cases annually was 3073 (interquartile range: 2774, 3242). We observed that 4641 (15.2%) were seen by radiation oncology within 6 months after radical
prostatectomy, of which 2377 (51.2%) were treated with ART. For 2003–2010, 16.9% were treated with SRT within 24 months according to the definitions above. Overall, 4923 (16.2%) cases were treated with radiotherapy within 24 months, of which 2424 (49.2%) received ART. For 2003–2010, 53.9% received SRT.

Adoption of Early Radiation Oncology Consultation after Radical Prostatectomy

Table 1 illustrates that the proportion of radical prostatectomy cases seen by radiation oncology within 6 months after radical prostatectomy doubled over the study decade, ranging from 10.7% in 2003–2004 to 21.7% in 2011–2012 ($P < 0.0001$). The annual percentage difference was largest in 2009–2011 (3.4%). By comparison, the proportion of radical prostatectomy cases seen by radiation oncology within 24 months remained at 32.3% ± 1.4%.

Adoption of Adjuvant Radiotherapy after Radical Prostatectomy

ART rates among all radical prostatectomy cases nearly doubled over the study period, ranging from 6.2% in 2003–2004 to 11.0% in 2011–2012 ($P < 0.001$). Earlier radiotherapy use was seen to parallel the increasing proportions of patients seen within 6 months after radical prostatectomy. There was a similar gradual rise in ART rates in 2003–2007, followed by an inflection point, indicating a more rapid rate of change in 2009–2011. Furthermore, among the 4641 patients seen by radiation oncology within 6 months of radical prostatectomy for consideration of ART or SRT, ART use remained at 51.0% ± 3.0%. Among all radical prostatectomy patients, although there were significant trends in ART, SRT rates within 24 months remained stable at 8.4% ± 0.4%. Overall, the total proportion receiving radiotherapy within 24 months increased from 14.1% in 2003–2004 to 17.7% in 2009–2010 ($P < 0.0001$). These radiotherapy trends remained consistent when we carried out sensitivity analyses of radiotherapy initiation within 4, 6, and 8 months after radical prostatectomy as definitions of ART.

Table 1
Trends in post-radical prostatectomy radiation oncology consultation and adjuvant radiotherapy (ART) utilisation between 2003 and 2012

<table>
<thead>
<tr>
<th>Year of radical prostatectomy</th>
<th>N</th>
<th>Percentage of all radical prostatectomy cases seen by radiation oncology within 6 months</th>
<th>Relative risk (95% confidence interval)</th>
<th>Percentage of all radical prostatectomy cases receiving ART</th>
<th>Relative risk (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003–2004</td>
<td>5260</td>
<td>10.7</td>
<td>Reference</td>
<td>6.2</td>
<td>Reference</td>
</tr>
<tr>
<td>2005–2006</td>
<td>6470</td>
<td>13.1</td>
<td>1.23 (1.11–1.36)</td>
<td>6.2</td>
<td>0.99 (0.86–1.14)</td>
</tr>
<tr>
<td>2007–2008</td>
<td>6714</td>
<td>13.8</td>
<td>1.29 (1.17–1.43)</td>
<td>7.3</td>
<td>1.14 (1.03–1.35)</td>
</tr>
<tr>
<td>2009–2010</td>
<td>6125</td>
<td>16.9</td>
<td>1.58 (1.44–1.74)</td>
<td>9.0</td>
<td>1.45 (1.27–1.65)</td>
</tr>
<tr>
<td>2011–2012</td>
<td>5878</td>
<td>21.7</td>
<td>2.03 (1.86–2.23)</td>
<td>11.0</td>
<td>1.77 (1.56–2.01)</td>
</tr>
<tr>
<td>All cases combined</td>
<td>30 447</td>
<td>15.2</td>
<td>—</td>
<td>7.8</td>
<td>—</td>
</tr>
</tbody>
</table>

Utilisation Kinetics of Radiation Oncology Consultation and Radiotherapy after Radical Prostatectomy

Figure 1 shows the proportion of cases seen by radiation oncology and the proportion treated with radiotherapy as a function of time since prostatectomy. These cumulative rates rise rapidly in the first 6 months after radical prostatectomy, then gradually flatten, but do not reach a true plateau owing to late recurrences. The shape of the time-to-radiation oncology consultation curve varies for radical prostatectomy years; the divergence is apparent for the first 6 months after radical prostatectomy; there is a clear trend towards earlier radiation oncology consultation, most pronounced in later time periods (2007–2008, 2009–2010, 2011–2012). Later curves also appear to trend toward plateau at progressively higher rates of radiation oncology consultation (Figure 1A). Similarly, time-to-treatment curves show earlier initiation of radiotherapy after radical prostatectomy, with a more rapid increase in the proportion treated within 6 months in later years. Ultimately, the earlier curves appear to converge to the same long-term radiotherapy rate (Figure 1B).

Trends in Patterns-of-Care after Radical Prostatectomy in Relation to the State of Knowledge

Figure 2 shows a timeline for temporal trends in radiation oncology consultation and ART utilisation in Ontario over the study period in relation to dates of publication of trials and guidelines. Between 2003 and 2006 there was a gradual increase in early radiation oncology consultation from 9.8% to 13.2%, whereas ART rates remained around 6%. Starting in 2004, three clinical trials reported biochemical disease-free survival benefit with the use of ART compared with observation for high-risk pathological features [1,2,4,5]. The proportion of early radiation oncology consultation then stabilised at 13.0% in 2006–2007. Starting in 2009, early radiation oncology consultation rates increased rapidly and by 2012 the rate was 21.8%. Similarly, ART rates rose from 7.3% in 2007–2008 to 11.0% in 2011–2012. These rapid changes coincided with the release of 2008 GUROC and CCO guidelines, recommending early radiation oncology referral for high-risk pathological features after radical prostatectomy [17–19]. Also in 2009, the
first clinical trial long-term follow-up data were reported, showing an overall survival benefit for men randomised to ART [8].

Discussion

The main findings of this population-based study were that between 2003 and 2012, adoption of early radiation oncology consultation after radical prostatectomy in Ontario increased. The increasing trend began shortly after trial and guideline publications. The doubling from 10.7% to 21.7% in radical prostatectomy cases receiving early radiation oncology consultation was temporally associated with a rise in ART utilisation from 6.2% to 11.0%. ART rates remained proportional to radiation oncology referral rates over the study decade (51.0% ± 3.0%), suggesting that improvement in access to early radiation oncology opinion affect patient management. Our results unequivocally showed a change in practice and there is a strong association with dissemination of evidence and guidelines. This provides an indication of quality of care.

We explored continuous time trends associated with two steps in the care pathway of patients after prostatectomy: (i) radiation oncology referral and (ii) subsequent radiotherapy. Radiation oncology referral is an end point that directly measures the effect of reported advances in medical knowledge. Dissemination of clinical trials and guidelines was associated with a doubling in early radiation oncology consultation rates. Adoption occurred gradually before reaching an inflection point indicating a more rapid rise shortly after 2008. One reason that early radiation oncology consultation has not been more rapidly adopted may be that although practice guidelines urge consideration for ART, they do not offer guidance as to whether ART or SRT is more appropriate. The period of greatest absolute increase in early radiation oncology referrals and ART utilisation followed publication of the long-term SWOG 8794 study results in 2009, which showed a survival benefit from ART [8]. Trends in radiation oncology referral and subsequent ART use in 2009—2012 highlights concordance between clinical practice the available evidence at that time. Since then, however, additional long-term randomised controlled trial data have been reported and do not show overall survival benefits of ART [3,25]; the effect of these reports on patterns of practice will require that these patterns be systematically studied by repeating this type of research at periodic intervals in the future. Nevertheless, the significant increase in early post-prostatectomy radiation oncology referral rates observed is unlikely to reflect inappropriate care, but probably reflects improvement in effectiveness of health services and access to care.

Fig 1. Radiotherapy (RT) consultation and treatment as a function of time since radical prostatectomy (RP). Proportion of cases treated with radical prostatectomy in Ontario between 2003 and 2012 that were (A) seen by radiation oncology (RO) and (B) treated with radiotherapy (biannual rates by year of radical prostatectomy).
We considered other confounding factors that might have contributed to the observed time trends other than dissemination of evidence, such as theoretical changes in case mix, earlier detection of recurrences with ultra-sensitive PSA testing, changes in radiotherapy wait times in Ontario, or increased collaboration between urologists and radiation oncologists. We were unable to assess changes in case mix directly without systematic stage and risk groupings to describe the appropriateness of case selection for radiotherapy. Historic data on pathology findings at radical prostatectomy in Ontario across the study period were not available, but Table 2 shows that the proportion of prostatectomies with high-risk features seemed relatively stable among the different provinces and study periods. A US-based report found that patients with high-risk disease are increasingly undergoing prostatectomy [29]. However, most of the move towards higher risk patients receiving radical prostatectomy is a recent phenomenon, and it is not likely that this substantially contributed to trends we observed in the earlier years of our 2003–2012 study period. Particularly in view of trends in radical prostatectomy management, the merit of postoperative radiotherapy is becoming a central issue. The goal of the present study was to document changes in practice patterns after radical prostatectomy and the trends observed were consistent with improved access to radiotherapy after radical prostatectomy. This is good news for patients with high-risk disease who may benefit from ART.

Interpretation of study findings is also limited by a lack of information available in retrospective administrative data regarding potential confounding factors. For example, a lack of PSA data increases the risk of misclassification of ART versus SRT. Furthermore, using a time-based definition may theoretically be more sensitive to fluctuations in waiting times for radiotherapy after radiation oncology consultation, leading to misclassification of ART as SRT when waiting times are longer. However, the clear increase in early radiation oncology referral rates observed would not have been

![Fig 2. Trends in early radiation oncology (RO) consultation and adjuvant radiotherapy (ART) usage after radical prostatectomy (RP). The histogram illustrates temporal changes in the annual proportion of patients receiving a radiation oncology visit within 6 months after radical prostatectomy in Ontario between 2003 and 2012. Consultations resulting in ART are shown as dark grey bars, and other consultations as pale grey bars. Dates of key trials and publications are shown for reference.](image)

<table>
<thead>
<tr>
<th>Region</th>
<th>Period</th>
<th>Radical prostatectomy cases (n)</th>
<th>Adverse pathology (% of radical prostatectomy)</th>
<th>Radiation oncology referral within 6 months (% of radical prostatectomy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manitoba [27]</td>
<td>2003–2008</td>
<td>1080</td>
<td>50.6</td>
<td>14.3</td>
</tr>
<tr>
<td>Alberta [28]</td>
<td>2005 versus 2012</td>
<td>658 versus 485</td>
<td>44.8 versus 42.6</td>
<td>13.7 versus 22.9</td>
</tr>
</tbody>
</table>

* % of radical prostatectomy cases with adverse pathology.

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influenced by such radiotherapy wait time trends. Also, a lack of PSA data increases the risk of misclassification of curative versus palliative-intent settings for radiation oncology consultation, but any bias towards over-representation of radiation oncology consultations for curative prostate-bed radiotherapy is probably compensated by effects of competing risks, such as death, in the cumulative utilisation curves. Additionally, administrative data may be missing information on patients who left the province for radiotherapy; however, these few cases would not significantly bias our results.

Despite these methodological limitations, this large study is the first post-prostatectomy patterns of care analysis to date describing time trends in both referral and treatment that spans a decade relevant to publication of major trials and guidelines. The robustness of our study is based on comprehensive, reliable registries for the entire population of interest, thus minimising referral bias. Investigating both referral and treatment steps in the care path after radical prostatectomy made it possible to infer whether variations in radiotherapy use reflect non-referral or decisions made after radiation oncology consultation. Finally, we represented trends as a function of time since prostatectomy and across time periods. The former visually shows care timelines after radical prostatectomy, whereas the latter identifies categorical changes in practice. This provides timely insight into prostate radiotherapy trends given the evolving evidence and variability in practice.

By comparison, Table 2 shows that there is variability in radiation oncology referral among the provinces. US-based studies have found stability or decline in the use of ART during the same time period that we showed increased use in Canada [30–32]. Reluctance to adopt this practice change could be due to an ongoing debate of ART versus SRT. There may also be differences in patient preference, or under-ascertainment of treatment [33]. Presumption of equivalence for early SRT and ART must be viewed critically until comparative randomised trials are completed, and this is reflected in recent joint guidelines from the European Association of Urology and the European Society for Medical Oncology [34,35] as well as the American Urological Association and American Society for Radiation Oncology [22], to offer and carefully discuss postoperative radiotherapy. Future changes in practice patterns following guideline publication in other health care systems will be of interest.

Optimal outcomes for patients having adverse pathology after radical prostatectomy require optimum quality of care. Although randomised trials compare the efficacy of ART versus SRT, population-based studies are also necessary to evaluate the impact of knowledge on practice, providing an indication of the quality of care received. Literature on the dissemination of innovations suggests that dissemination of evidence may have variable effects on practice [36]. Overall, the practice of Canadian urologists seems to have been guided by trials and evidence-based guidelines. Further investigation of variability in practice, and factors affecting radiation oncology referral and radiotherapy use after radical prostatectomy is both necessary and planned.

Conclusions

We conclude that there was an increase in early post-prostatectomy radiation oncology referral and ART use in Ontario from 2003 to 2012, following publication of trials and guidelines. Increases in radiotherapy use after radical prostatectomy seem to be driven by patient access to an early radiation oncology opinion.

Timely discussion of radiotherapy options in light of complex and evolving evidence is essential for patients to make informed decisions about their care. As results of trials comparing ART and SRT become available, knowledge of current practice patterns in Ontario will inform initiatives to improve the quality of care for prostate cancer patients. In the meantime, referring and treating physicians must be vigilant to ensure patients have the opportunity to consider all of their treatment options after prostatectomy.

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