# *Does prolonging the time to testicular cancer surgery impact long-term cancer control: a systematic review of the literature*

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***Background:*** *The wait times for urological cancer surgeries in Canada are beyond those recommended by the Canadian Association of Surgical Oncology. Prolonged wait times have a negative impact on patient quality of life but the effect on long-term cancer control is controversial. We conducted a systematic review of the testicular cancer literature to examine the best available evidence addressing the following key questions:*

- *What is the reported time interval for testicular cancer patients from the decision to operate until the day of testicular cancer surgery?*
- *Are there recommendations/guidelines in the urological cancer literature and, if so, how do the Canadian times compare?*
- *Is there a known association between duration of wait time beyond the recommended standard and clinical outcome (i.e. recurrence free survival, overall survival)?*

***Methods:*** *A structured literature search of Medline, Pubmed, CINAHL, EMBASE, the Cochrane Database of Systematic Reviews, the Cochrane Database of Abstracts of Reviews of Effects, Healthstar and Google Scholar from January 1980 to September 2005 was conducted for published epidemiological studies and international guidelines/ consensus documents that evaluated surgical wait times for testicular cancer. Data extracted from eligible studies included median time to diagnosis and to testicular cancer surgery.*

***Results:*** *Five studies evaluating different components of wait times (e.g. delay in diagnosis, delay in orchiectomy) in testicular cancer patients were identified, four of which measured the impact of prolonged delays on relapse free and overall survival. Differences in study data availability, method of analysis and wait time definitions precluded statistical pooling of the findings. In one study from the United Kingdom, median wait time was 30 days from general practitioner referral to surgery and 4 days from diagnosis to surgery. No Canadian studies specific to testicular cancer were identified. The association between surgical delay and clinical outcomes remained controversial where only one of five epidemiological studies reported an association between treatment delay and relapse free and overall survival*

***Conclusions:*** *Even though the association between surgical delay and disease related clinical outcomes remains controversial, there is an ongoing concern that the psychological impact of prolonged waiting for urological cancer surgery could negatively impact patient outcomes. Additional research is needed to identify the current wait times for testicular cancer in Canada and to develop guidelines and recommendations on what appropriate wait times should be. To address these important issues, the surgical wait times (SWAT) initiative is mandated to provide the necessary guidance and recommendations to the federal and provincial governments. Through a partnership between the key stakeholders, it is the vision of SWAT to ultimately improve the care and quality of life of cancer patients.*

**Key Words:** testicular cancer, surgery, wait time, delay

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## Introduction

Cancers of the testes consist of a clinically and morphologically heterogenous group of tumors with the most common being germ cell tumors (GCT).[1] GCT are the most common solid malignancy in males between the ages of 20 to 35.[1] The two main histologic subgroups of GCT are seminoma and non-seminoma, each contributing to 50% of the total number of new cases.[1] In Canada, there were 850 new cases and 30 deaths from the disease in 2005 and the incidence appears to be increasing by approximately 1.8% per year.[1,2] If managed correctly at all stages of disease, GCT are highly curable with the appropriate use of either radiation therapy, chemotherapy or surgery.[1] As recommended by the European Germ Cell Cancer Consensus Group, radical orchiectomy should be performed prior to any further treatment.[3]

Once a patient makes a decision for surgery, certain reasonable expectations arise, an important one being the wait time. There is evidence in the literature that the median wait time from referral to surgery for urological cancers including GCT is beyond the 14-day duration considered by the Canadian Society of Surgical Oncology (CSSO) to be acceptable.[4,5] Total wait time from referral to surgery has many components such as referral to first visit, first visit to main treatment decision, main treatment decision to surgery and receipt of pathology report to orchiectomy.[4] Two key components of this sequence that urological surgeons may be able to influence are time to receipt of pathology and diagnostic imaging information in order to recommend surgery and time from the decision to operate until the actual procedure. Therefore, reducing the time interval within these two periods may have a positive impact on the patient in terms of stress level and other psychosocial factors. It has been well documented that a prolonged wait time and long waiting lists can have a negative impact on almost all the dimensions of patient quality of life.[6-8]

The CSSO recommends that the time from treatment decision to all types of cancer surgery should not exceed 14 days.[5] However, many of the published epidemiological studies have focused on the impact of delayed diagnosis on relapse free and overall survival.[9,10] Therefore, the true impact of surgical delay on testicular cancer control remains controversial and what the appropriate wait time should be is currently unknown.

To address these issues for the key urological disease sites; prostate, bladder, kidney and testes, a Canadian surgical wait times (SWAT) initiative was recently undertaken. The SWAT initiative is composed of a steering committee and a scientific advisory committee. The SWAT initiative, whose members consist of urologic oncologists, surgeons and methodologists is mandated to review the current literature on the surgical wait times for urologic cancers and then develop a consensus document that can serve as a guide for patients, physicians and other key stakeholders in the Canadian health care system. To begin this process, the SWAT steering committee undertook a review of the testicular cancer literature to determine what the recommendations are on appropriate wait times for orchiectomy and to quantify the overall risk of disease recurrence and overall survival in patients who have wait times beyond the recommended threshold. In this study, the results of the systematic review of the literature reporting the impact of prolonged wait time on testicular cancer clinical outcomes are described.

## Methods

### *Objectives*

We conducted a systematic literature review to examine the best available evidence addressing the following key questions:

- What is the reported time interval for testicular cancer patients from the decision to operate until the day of testicular cancer surgery?
- Are there recommendations/guidelines in the urological cancer literature and, if so, how do the Canadian times compare?
- Is there a known association between duration of wait time beyond the recommended standard and clinical outcome (i.e. recurrence free survival, overall survival)?

### *Data sources, study selection and data extraction and synthesis*

We performed a structured literature search of Medline, Pubmed, CINAHL, EMBASE, the Cochrane Database of Systematic Reviews, the Cochrane Database of Abstracts of Reviews of Effects, Healthstar and Google Scholar from January 1980 to September 2005 for published epidemiological studies and international guidelines/consensus documents that evaluated surgical wait times for testicular cancer. The following inclusion criteria were used: 1) The document was available as a full report; 2) The document was developed in North or South America, Western Europe, Australia or New Zealand; 3) Patients undergoing testicular cancer surgery must have been considered and 4) The primary outcome of interest for epidemiological studies must been the association

between time to treatment and clinical outcomes. Care was undertaken to avoid the inclusion of duplicate publications.

We conducted searches of the listed databases in July, August and September 2005. One member of the working group conducted the searches. Eligible studies were selected by the first member and compared with results from a search by another member. Data were abstracted by one member and confirmed by a second person. We obtained full copies of all primary study reports, as well as working tables that summarized the key study characteristics and data.

Since the definitions of wait time varied widely among the studies, those that characterized it differently from "the initial surgical consultation until the day of surgery" were also evaluated. We then compiled the key characteristics of each study in summary tables. Studies evaluating the natural history of testicular cancer were also considered and we made particular note of those that placed the patients into risk groups. All risk ratios from the accepted epidemiological studies were examined for the possibility of statistical pooling via meta analytic techniques.

## Results

### *Wait time for surgery*

The majority of the studies in the testicular cancer literature measured delay from the onset of symptoms until diagnosis. Only three studies reporting wait times for cancer surgery were identified. Differences in available study data, method of analysis and wait time definitions precluded statistical pooling of the data. Wait time definitions consisted of general practitioner (GP) referral to surgery, symptoms to surgery and diagnosis to surgery. As a result, median wait times ranged from 4 days from diagnosis to surgery to 75 days from onset of symptoms to orchiectomy, Table 1. There was only one Canadian study that evaluated wait times for all urological surgeries in the province of Ontario.[4] Definitions of wait times were slightly different, but their findings were internally consistent. Using data from 58 patients undergoing urological surgery between January to May 2000, Simunovic et al determined a median wait time from referral to surgery of 64 days.[4] Unfortunately in their study, a breakdown of the urological tumor types was not provided, making it impossible to estimate the delay in the testicular cancer subgroup.

In a study by Subramonian and colleagues from the United Kingdom, a more detailed breakdown of wait time for orchiectomy was provided.[11] The median time from GP referral to surgery was 30 days and from diagnosis to surgery 4 days, Table 1. In an older study also from the United Kingdom, Chilvers et al reported a median time of 75 days from symptoms to orchiectomy.[12] Due to the lack of published Canadian data, it is difficult to ascertain what the true wait times for Canadian testicular patients are. However there is an indication that wait times may be beyond the limit as recommended by expert groups.[13]

### *Wait time guidelines and recommendations from the literature*

Two professional bodies and one group of investigators developed recommendations for maximum wait time for cancer surgery, Table 2. The Canadian Society of Surgical Oncology (CSSO) and the United Kingdom National Health Service both made similar recommendations where the maximum wait times for all cancer surgeries from diagnosis to treatment should be 2 weeks as stated by the former group and 4 weeks from the latter.[5,14] The position statement of the CSSO states that cancer patients should be seen in consultation within 2 weeks of referral and that surgery should be initiated within 2 weeks of any preoperative tests.[5] The United Kingdom National Health Service specifies in its "Cancer Plan" that there should be a maximum wait of 2 weeks from the time of the GP referral to the time of a specialist's assessment; a maximum 1 month wait from diagnosis and treatment; and a maximum 2 month wait from an urgent GP referral to actual treatment.[14] These

TABLE 1. **Reported wait times for testicular cancer surgery in various countries**

| Reference | Country | No. patients (n) and year | Wait time definition | Median duration |
|---|---|---|---|---|
| Simunovic[4] | Canada | n = 58; Jan-May 2000 | Referral to surgery | 64 d[a] |
| Subramonian[11] | United Kingdom | n = 40; prior to 2000 | Diagnosis to surgery | 4 d |
| | | | GP referral to surgery | 30 d |
| Chilvers[12] | United Kingdom | n = 257; 1980-1986 | Symptoms to surgery | 75 d |

[a]Considered all urological cancer surgeries and did not distinguish by disease site.

TABLE 2. **Recommended maximum wait times from the literature**

| Reference | Wait time definition | Recommended maximum wait time | Type of surgery |
|---|---|---|---|
| CSSO[5] | Referral to consultation | 2 weeks | All cancer surgeries |
| United Kingdom National Health Service[14] | GP referral to specialist assessment | 2 weeks | All cancer surgeries |
| | Diagnosis to treatment | 1 month | All cancer surgeries |
| | Urgent GP referral to treatment | 2 months | All cancer surgeries |

recommendations are for all cancer types, and there are no particular guidelines for orchiectomy. In summary, concise recommendations regarding wait times for urological cancers and testicular malignancies in particular are lacking in the literature.

### *Recommendations on the availability of diagnostic imaging and pathology data*

A key component in the delivery of effective and efficient surgery for all types of urological cancer is the timely availability of diagnostic imaging results and disease pathology. The national and international literature was also examined to identify recommendations for the maximum time interval for these two important components of urological cancer surgery. Two documents were identified, one from the National Institute of Clinical Excellence (NICE) of the United Kingdom and the second from the Canadian Medical Association (CMA).[15,16] NICE recommends that information required for accurate disease staging and pathology results should be available within 7 days in cases where clinical examination suggests the presence of cancer.[15] The CMA in their report recommended that diagnostic imaging results should be made available within 24 hours for emergency cases, 7 days for urgent cases and 30 days for semi-urgent cases. For routine cases, defined as situations involving minimal pain, dysfunction or disability (i.e. elective cases), the results should be made available within 7 days of the scheduled time frame in situations where follow up imaging is required.[16]

### *Is there an association between wait time and clinical outcomes?*

One of the main objectives of the current study was to evaluate the epidemiological literature that measured the association between prolonged wait times and patient clinical outcomes. There were no studies measuring the association between clinical outcomes and delay from the decision to operate until the actual surgical procedure. It immediately became apparent that most of the studies (i.e. four of five) evaluated overall delay in diagnosis, which consists of two components; patient associated delay and physician-associated delay due to factors such as incorrect diagnosis. Therefore, this section of the current study used the association between delay in diagnosis and clinical outcomes as a surrogate measure for the impact of surgical delay on relapse free and overall survival. The hypothesis being that lack of association between overall delay and clinical outcomes would suggest that even shorter delays from the decision to operate until the actual procedure would also not impact relapse free and overall survival.

Five published studies were identified, Table 3. It is important to note that all of the studies evaluated patients treated before the 1990s. All of the studies used retrospective cohort designs with the primary outcome being either the proportion of patients developing metastatic disease, disease stage at diagnosis, relapse free and overall survival. Wishnow et al placed 154 patients into groups who received orchiectomy within 30 days (Group 1) of symptoms or beyond 30 days (Group 2).[17] After at least 2 years of follow up, metastatic disease developed in 57% of Group 1 patients compared to 81% in Group 2 (crude $p < 0.001$). At 2 years follow up, 98.5% of patients who received surgery within 30 were alive compared to 87.6% in those who received surgery after 30 days (crude $p = 0.0072$). The investigators concluded that performing prompt orchiectomy after the offset of testicular symptoms can have a major effect on the morbidity of testicular cancer by reducing the need for systemic chemotherapy or major surgery.[17] Notwithstanding, it is important to note that they only reported crude unadjusted p-values and imbalance of known prognostic factors such as disease stage may have confounded the results. In another study, Bosl et al identified a statistically significant association

TABLE 3. **Epidemiological studies evaluating the association between treatment delays and cancer control rates**

| Reference | No. patients[a] | Years | Key groups evaluated | Key outcome |
|---|---|---|---|---|
| Wishnow[17] | 154 | 1983-1986 | Gp 1: delay ≤ 30 d versus<br>Gp 2: delay > 30 d | Metastatic disease:<br>57% versus 81%; p < 0.001<br>Overall survival at 2 years:<br>98.5% versus 87.6%; p = 0.0072[b] |
| Harding[18] | 454 | 1975-1989 | Gp 1: delay < 45 d versus<br>Gp 2: delay 45 to 90 d versus<br>Gp 3: delay > 90 d | Metastatic disease:<br>62% versus 64% versus 57%;<br>p = 0.807<br>Overall survival at 5 years:<br>87% versus 78% versus 75%;<br>p = NS[c] |
| Moul[19] | 58 | 1979-1987 | Gp 1: delay ≤ 112 d versus<br>Gp 2: delay > 112 d | Overall survival at 5 years:<br>89.6% versus 78.9%; p = 0.262[b] |
| Bosl[20] | 303 | 1941-1978 | Stage I delay = 75 d versus<br>Stage II delay = 101 d versus<br>Stage III delay = 134 d;<br>p = 0.017 d | Impact on clinical outcomes<br>not measured |
| Cilvers[12] | 257 | 1980-1986 | Gp 1: delay ≤ 49 d versus<br>Gp 2: delay 50 d to 99 d versus<br>Gp 3: delay ≥ 100 d | Relapse free survival reduced<br>in patients with delay<br>≤ 49 d; p < 0.05<br>In stage I marker negative cancers,<br>no significant relation between<br>relapse free survival and delay |

NS = not significant. Note; only the study by Wishnow et al, evaluated time from symptoms to surgery. All of the other studies evaluated time from symptoms to diagnosis.
[a]All studies used retrospective cohort designs.
[b]Crude unadjusted p-value. Did not adjust for imbalance of know prognostic factors such as disease stage.
[c]p-value adjusted for know prognostic factors.

where patients with prolonged delays in the diagnosis of testicular cancer tended to have more advanced stage disease, Table 3.[20] However, they did not measure the impact of this difference on overall survival.

In contrast to the above findings, which indicated a potential risk with delay, the studies by Harding et al,[18] and Moul et al,[19] failed to detect differences in the development of metastatic disease and overall survival in patients who received an early diagnosis of testicular cancer compared to beyond 3 months, Table 3. To further complicate the association, Cilvers et al, in a retrospective cohort study involving 257 patients identified an inverse relationship between time from onset of symptoms to orchiectomy and clinical outcomes where patients within the 49 day treatment group had a reduced relapse free survival compared to patients in the beyond 49 day group.[12] This difference was attributed to the possibility that faster growing tumors are more likely to produce symptoms leading to medical consultation and orchiectomy. When the same investigators evaluated the association between delay in diagnosis and relapse free survival in stage I marker negative patients, there was no difference in outcome between patients diagnosed within 49 days of symptoms compared to beyond 49 days.[12] In summary, the evidence evaluating the impact of long wait times on clinical outcomes is conflicting. Furthermore, the studies did not assess patients diagnosed after 1990 when more modern chemotherapy became available to treat recurrent disease.

## Discussion

We conducted a systematic review of the literature to identify current wait times for testicular cancer surgery, recommendations on what the maximum wait time should be and to assess the possible association between surgical delays and patient clinical outcomes.

We were unable to find published Canadian data on the average wait time for testicular cancer surgery. Simunvic et al, reported a median of 64 days for urological cancers in the province of Ontario, but did not provide a breakdown for the individual tumor types.[4] The most recent data was from the United Kingdom and it revealed that wait times for orchiectomy are acceptable in that country. The median wait time from GP referral to surgery was 30 days and 4 days from diagnosis to surgery.[11] These times are consistent with both the United Kingdom National Health Service and CSSO recommendations.[5,14] In Canada, we should strive for similar wait times for testicular cancer surgery. Additional Canadian research is needed to quantify the wait time for the individual urological cancers in order to identify the problem areas.

Recommendations on maximal wait times or standards for acceptable surgical delay in testicular cancer were also not available, suggesting the need for guidelines specific to the individual urological cancer disease sites. Objective benchmarks for appropriate waits do exist in Canada,[5] but these recommendations are not specific to urological cancer in general and testicular cancer in particular. Therefore, an immediate priority is to develop benchmarks based on expert consensus following a review of the literature.

The association between prolonged wait times for either diagnosis or treatment and recurrence free and overall survival is controversial. Although one study concluded that prompt orchiectomy reduces the risk of metastatic recurrence and prolongs overall survival,[16] there was other evidence suggesting either no impact of delays beyond 90 days or even a worse outcome in patients with shorter delays.[12,18,19] This latter finding is probably related to the fact that patients with more aggressive tumor are more likely to be symptomatic and seek early treatment.[12]

The findings of this review revealed that there is insufficient evidence to determine the optimal timing for orchiectomy from the decision to operate. Therefore, more well designed epidemiological studies are needed to examine the association between wait time and clinical outcome with the ultimate objective being the identification of a threshold that would assist in the development of surgical guidelines for informed health policy decision making.

One of the key components to efficient urological cancer surgery is the timely availability of diagnostic imaging and disease pathology. The report from NICE in the United Kingdom was specific to all urological cancers and recommended that accurate disease staging and pathology results should be available within 7 days in cases where clinical examination suggests the presence of cancer.[15] The recommendations from the CMA were not specific to urological cancers. Nevertheless, their general recommendations for diagnostic imaging were within 24 hours for emergency cases, 7 days for urgent cases and 30 days for semi-urgent cases. For routine cases, the results should be made available within 7 days of the scheduled time frame in situations where follow up imaging is required.[16]

The clinical impact of prolonged surgical delay remains controversial.[11] However, the impact on patient health associated with psychological stress resulting from prolonged waiting has been established. There is extensive data indicating that delays for urological cancer surgery have significant effects on psychological well being, and reduced waiting times may result in a decrease in psychological morbidity.[6-8] Therefore, measuring current wait times for testicular cancer surgery and developing a strategy to reduce these wait times to acceptable levels will have a profound positive impact on patient stress and quality of life. This is particularly important in testicular cancer because it is highly curable and is the most common cancer in young men between the ages of 20 to 35.[1,2]

Another important factor that needs to be considered in addition to wait time is quality of care during and after urological cancer surgery. There is extensive evidence in the literature suggesting that post operative surgical complications are lower in high-volume centers and if performed by surgeons who perform a high number of such procedures.[22-24] Therefore, health policy decision makers need to consider overall quality of care when establishing bench marks for surgical wait times.

In conclusion, the findings of our systematic literature review revealed that the national and international guidelines recommend a maximum wait time for cancer surgeries such as orchiectomy between 2 to 4 weeks. Even though the association between surgical delay and disease recurrence is controversial, there is a concern among some clinicians that the psychological impact of prolonged waiting could negatively impact patient outcomes.[20] To address these important issues, the SWAT initiative is mandated to provide the necessary guidance and recommendations to the federal and provincial governments. Through a partnership between the key stakeholders, it is the vision of SWAT to ultimately improve the care and quality of life of cancer patients. □

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