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Evaluating delays in patients treated with post-operative radiation therapy for head and neck squamous cell carcinoma

Ravi Marwah,[1] Daniel Goonetilleke,[1] Justin Smith[1,2] and Madhavi Chilkuri[1,2]

1 Townsville University Hospital, Townsville, Queensland, Australia
2 James Cook University, Townsville, Queensland, Australia

R Marwah MBBS; **D Goonetilleke** MBBS; **J Smith** MBBS(Hons), MPH; **M Chilkuri** MD, FRANZCR, MPH.

Correspondence
Dr Madhavi Chilkuri, Townsville University Hospital, 100 Angus Smith Drive, Douglas, Qld 4814, Australia.
Email: madhavi.chilkuri@health.qld.gov.au

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Abstract

Introduction: Delays in commencing post-operative radiation therapy (PORT) and prolongation of overall treatment times (OTT) are associated with reduced overall survival and higher recurrence rates in patients with head and neck squamous cell carcinoma (HNSCC). The objective of this study was to evaluate treatment delays, factors contributing to those delays and to explore strategies to mitigate them.
Methods: This retrospective study included patients with mucosal HNSCC at Townsville University Hospital treated with curative intent surgery and PORT between June 2011 and June 2019. The proportion of patients who experienced delays in commencing PORT (>6 weeks) and OTT were evaluated and reasons for these delays were explored.
Results: The study included 94 patients of which 70% experienced PORT delay. Surgery at an external facility (81% vs 56%, $P = 0.006$) and longer post-operative length of stay ($P = 0.011$) were significantly associated with a higher incidence of PORT delay. Aboriginal and Torres Strait Islander patients had a higher rate of PORT delay (89% vs 68.2%, $P = 0.198$). Significant delays were noted from time of surgery to radiation oncology (RO) consult and from RO consult to commencement of radiation treatment.
Conclusion: This study demonstrates that the prevalence of PORT delay for patients with HNSCC remains high with room for improvement. Potential strategies to improve delays include developing effective care coordination, addressing specific needs of Indigenous patients, implementing reliable automated tracking and communication systems between teams and harnessing existing electronic referral systems.

Key words: head and neck cancer; post-operative radiotherapy; radiation therapy; treatment delays.

Introduction

Head and neck cancers include cancers of the pharynx, larynx, paranasal sinuses, nasal and oral cavity, with the most common histological type being squamous cell carcinoma.[1] Advanced stage head and neck squamous cell carcinoma (HNSCC) is managed curatively with primary surgery and post-operative radiation therapy (PORT) or chemoradiation.[2]

Although not randomised, several studies have demonstrated that delay in commencing PORT is associated with reduced survival and higher recurrence rates.[3–5] Therefore, guidelines nationally and internationally recommend commencing PORT within 6 weeks from surgery.[6–8] Time to PORT ≤6 weeks has also been proposed as a quality indicator for national benchmarking in several countries.[3,9–10] However, there is wide variation in its adherence, with PORT delay rates of 55.7%[9] and 61%[3] reported in two large national database studies conducted in the United States. A 2014 national audit of England and Wales also reported a median time to PORT of 50 days.[10] The only study evaluating PORT delays in Australia reported a delay rate of 62%.[11] In addition to delay in PORT, several studies have also linked prolonged overall treatment time (OTT; surgery to completion of PORT) to worse patient outcomes.[4,12,13] However, there is no consensus regarding an optimal time threshold, with studies reporting a wide range from 77 to

100 days.[14] Studies exploring reasons for PORT delay in the United States have identified a variety of associated factors such as black race, poor communication between care providers, longer post-operative lengths of stay, and receipt of surgery and PORT at different facilities.[9,15] However, there are no studies that have explored the reasons for PORT delay in Australia, which has a vastly different health system from the United States. The aim of this study was to evaluate treatment delays in patients with HNSCC, to determine the factors associated with these delays and to explore potential solutions to minimise these delays.

Methods

Study design

This was a single-institution retrospective chart review of patients over 18 years with mucosal HNSCC patients who received PORT between June 2011 and June 2019. All patients received PORT at Townsville University Hospital (TUH), a regional tertiary hospital in North Queensland, except one that was referred to another facility in the same region. Primary surgery was performed at either TUH or at one of two external metropolitan referral centres in Brisbane, approximately 1300 km south of Townsville. Patients with synchronous malignancies outside the head and neck region were excluded. This study follows an earlier study that reported quality indicators in head and neck cancer and identified time to PORT as an area for improvement at our institution.[16] Ethics approval for this study was granted by the Institutional Human Research Ethics Committee (HREC/QTHS/67801).

Data collection

Data were extracted from iEMR and MOSAIQ oncology management information system (OIMS) and entered into RedCap database. Data extracted included various patient characteristics including age, sex, date of birth, smoking status, ethnicity, Charlson Comorbidity Index and living distance from hospital. Tumour characteristics collected included tumour site, HPV status, TNM stage (AJCC 7th edition) and extranodal extension. Treatment details included date of diagnosis, dental workup requirement, surgery location, surgical margins, date of histopathology reporting, post-operative interruptions, post-operative length of stay, re-admission following surgery, date of post-operative referral, concurrent chemotherapy, interruptions of radiation therapy (RT) and the dates of various treatment time points. The date of referral was considered the date a post-operative referral letter was received. However, for those that were referred pre-operatively and had surgery at TUH, the date of referral was considered the date of the post-operative multidisciplinary team meeting when the patients were reviewed by a radiation oncologist.

Statistical analyses

Data were analysed using Stata V16 with the level of significance set at $P < 0.05$. Descriptive statistics were used to report the percentage of head and neck cancer patients with PORT delay (>42 days). Factors associated with PORT delays were analysed using a Chi squared test for categorical variables and Mann–Whitney *U* test for continuous variables.

Results

There were 94 patients included in the study. 70% (66/94) of patients were found to have a PORT delay (time to PORT >42 days) with the median time to PORT of 48 days.

Factors associated with PORT delay

Surgery at an external facility was significantly associated with PORT delay. The PORT delay rate at external facilities was 81% vs 56% at TUH ($P = 0.008$). Similarly, a longer post-operative length of stay was significantly associated with PORT delay (13 days vs 7.5 days, $P = 0.011$). Aboriginal and Torres Strait Islander patients had a higher rate of PORT delay than their non-indigenous counterparts although this difference was not statistically significant (89% vs 68.2%, $P = 0.198$) (Table 1).

Care processes associated with PORT delay

Median time from surgery to RO consult was 22 days, while median time from RO consult to PORT commencement was 26 days. Median time from RT planning to PORT start for the entire study cohort was 19 days.

Exploring these processes further, we found that of the entire study cohort, 53% (50/94) of patients had a surgery to RO consult time of greater than 3 weeks and 61% (57/94) had RO consult to PORT commencement greater than 3 weeks (Table 2) with 30% (28/94) of patients having greater than 3 weeks in both these processes. Similarly, 27% (25/94) of patients had a surgery to RO consult time of greater than 4 weeks and 30% (28/94) had RO consult to PORT commencement greater than 4 weeks. (Table 2) with 6% (6/94) of patients having greater than 4 weeks in both these processes. Given the delay associated with surgery at external facilities, care processes were further explored for this subset of patients. As shown in Table 3, median time of post-operative length of stay (13 days vs 7 days, $P = 0.03$), surgery to RO Consult (27 days vs 15 days, $P < 0.001$) and discharge to RO Consult time periods (12 days vs 6 days, $P < 0.001$) were all significantly longer with surgery at external facilities. Similarly, surgery to referral (19 days vs 12 days, $P < 0.001$), histopathology reporting

Table 1. Factors associated with PORT delay

Study cohort (n = 94)	PORT delay (>42 days)	P value
Patient characteristics		
Sex		
Male	56/78 (71.8%)	0.459
Female	10/16 (62.5%)	
Age†	59.4 ± 9.4 vs 59.3 ± 12.6	0.98
Ethnicity		
Aboriginal and/or Torres Strait Islander	8/9 (88.9%)	0.198
Not Aboriginal and/or Torres Strait Islander	58/85 (68.2%)	
Distance from Townsville Hospital		
≥200 km	40/53 (75.5%)	0.205
<200 km	26/41 (63.4%)	
Smoking status		
Current	39/51 (76.5%)	0.07
Former	23/33 (69.7%)	
Never	4/10 (40%)	
Charlson Comorbidity Index‡		
≤1	23/36 (63.9%)	0.291
>1	43/58 (74.1%)	
Tumour characteristics		
Tumour site		
Nasal cavity	2/3 (66.7%)	0.202
Oral cavity	41/53 (77.4%)	
Oropharynx	8/14 (57.1%)	
Hypopharynx	10/13 (76.9%)	
Larynx	5/11 (45.5%)	
Tumour stage		
Early stage	5/10 (50%)	0.139
Late stage	61/84 (72.6%)	
Extranodal extension		
Yes	25/31 (80.7%)	0.121
No	41/63 (65.1%)	
Treatment		
Surgery location		
External	43/53 (81.1%)	**0.008**
Internal	23/41 (56.1%)	
Surgical margins		
Positive	9/12 (75%)	0.698
Negative	57/82 (69.5%)	
Post-operative Length of Stay‡	13 days (12) vs 7.5 days (9.5)	**0.011**
Re-admission following surgery		
Yes	5/6 (83.3%)	0.448
No	59/86 (68.6%)	
Post-operative chemotherapy		
Yes	27/34 (79.4%)	0.142
No	39/60 (65%)	
Pre RT Dental work up required		
Yes	20/25 (80%)	0.212
No	46/69 (66.7%)	

†Mean ± SD, comparison to no PORT delay group.
‡Median (IQR), comparison to no PORT delay group.

to referral (13 days vs 1 day, $P < 0.001$) and referral to RO consult (7 days vs 0 days, $P < 0.001$) were also significantly longer with surgery at external facilities.

Table 2. PORT delays in relation to care processes

Time to PORT†	48 days (19)
PORT delay (>42 days)‡	Yes – 66 (70.2%) No – 28 (29.8%)
Surgery to RO Consult†	22 days (14)
• Surgery to RO Consult >3 weeks	50 (53.2%)
• Surgery to RO Consult >4 weeks	25 (26.6%)
RO Consult to PORT Start†	26 days (13)
• RO Consult to PORT Start >3 weeks	57 (60.6%)
• RO Consult to PORT Start >4 weeks	28 (29.8%)
RO Consult to Planning†	4.5 days (8)
Planning to PORT Start†	19 days (9)

†Median number of days (IQR).
‡Number of patients (%).

Table 3. PORT delay: surgery at TUH vs external facility

	TUH	External	Overall	P value
Post-operative length of stay†	7 days (10)	13 days (12)	10 days (10)	**0.003**
Surgery to RO consult†	15 days (10)	27 days (13)	22 days (14)	**<0.001**
Surgery to referral†	12 days (10)	19 days (12)	15 days (10)	**<0.001**
Surgery to histopathology†	8 days (6)	5 days (2)	6 days (4)	**<0.001**
Histopathology to referral†	1 days (7)	13 days (11)	8 days (14)	**0.001**
Referral to RO consult†	0 days (7)	7 days (9)	5 days (11)	**<0.001**
Discharge to RO consult†	6 days (10)	12 days (9)	10 days (9)	**<0.001**
RO consult to PORT Start†	27 days (12)	24 days (14)	26 days (13)	0.323

†Median number of days (IQR).
Statistically significant values are bold values.

Table 4. Overall treatment time

OTT	Number of patients (%)
<77 days	13 (13.8%)
78–84 days	21 (22.3%)
85–91 days	21 (22.3%)
92–98 days	15 (16%)
>98 days	24 (25.5%)

Overall treatment time

The median OTT was 86 days. OTT was greater than 13 weeks (91 days) in 41% (39/94) of patients, while 26% (24/94) of patients had OTT of greater than 14 weeks (98 days) (Table 4).

Factors associated with prolongation of OTT

Of all patients, 21% (20/94) had unplanned prolongation of their radiation treatment. The reasons included patient

non-compliance, machine breakdown and failure to compensate for unplanned treatment delays from public holidays and treatment starting mid-week. Only 14% (9/66) of patients with PORT delay (>42 days) were treated with altered fractionation.

Discussion

This study reports a PORT delay rate of 70% which is higher than rates reported in the literature (55.7–62%).[3,9,11] Our study found that surgery at an external facility was associated with a higher incidence of PORT delay compared with receiving surgery at TUH. Given patients requiring complex surgery are referred to an external facility, post-operative complications leading to prolonged post-operative stay (median; 13 days) in these patients are not unexpected. However, this alone was not the cause of delayed PORT. Patients had significantly longer delays in post-operative referrals and radiation oncology consults. Graboyes *et al*.[9] and Harris *et al*.[3] reported that patients who received surgery and PORT at different facilities were more likely to experience delayed PORT. Graboyes *et al*.[17] hypothesised that this may be due to insufficient care coordination and communication during care transitions, with providers facing the difficult task of reconciling differing electronic and paper-based health records. Janz *et al*.[18] suggested that patients experiencing care fragmentation may also be more likely to experience PORT delays due to their inability to receive initial radiation oncology consults during their surgical admission. Only one study to date has offered a potential solution for fragmentation of care.[19] This study utilised cancer care coordinators/navigators with multiple roles including systematically tracking referrals, as well as ensuring appointment scheduling and patient attendance, achieving a low PORT delay rate of only 14%.[19] While organisations might be reluctant to invest in such interventions due to cost, it is important to recognise the significant financial burden that is associated with poor patient outcomes.[20]

When care processes for all patients with delayed PORT were evaluated, we found that there were significant delays from time of surgery to RO consult and from RO consult to initiation of treatment, with several patients experiencing delay in both care processes. Post-operative complications, patient non-compliance and delayed/extensive pre-radiation dental extractions can contribute to delays from radiation oncology consult to PORT.[15] While these factors were noted in our study, there were other avoidable factors such as prolonged consult to planning, prolonged planning to treatment and failure to compensate for unscheduled treatment interruptions that impacted both delay in PORT commencement and OTT. We should recognise that while there will be unavoidable delays in at least some patients, avoidable delays must be minimised. A prospective randomised trial by Ang *et al*. found that time to PORT was greater than 42 days in only 9% of patients, and this was due to slow wound healing, fistula or bone exposure, laryngeal oedema or aspiration and poor compliance.[4]

For those that have had delays in commencement of PORT, attempts should be made to reduce the OTT. Retrospective studies have demonstrated an optimal OTT of 77–100 days[14] while analysis from a prospective randomised trial found inferior outcomes with OTT beyond 77–91 days, with OTT of >91 days especially detrimental when treatment initiation was delayed beyond 42 days.[4] With OTT greater than 91 days in 42% of our patient cohort, this is an area for improvement. Altered fractionation (accelerated radiotherapy, hyper-fractionation) has been shown to improve locoregional control with acceptable acute toxicities and comparable late toxicities when compared to conventional fractionation, although a survival benefit has not been established.[21–23] The Royal College of Radiologists (RCR) recommends compensatory measures (such as acceleration and/or increasing the dose per fraction) to minimise the effects of prolongation of treatment from unscheduled treatment interruptions.[24] As part of clinical benchmarking in radiation oncology to improve quality of care and clinical outcomes, prolongation of treatment times in RCR category 1 cancers (includes head and neck cancers) is monitored and reported nationally in Australia. In 2019, prolongation of treatment time by more than 2 days was found in 12.5% of patients though the institutions reporting this quality metric was low.[25] In the UK, this metric has been set at <5% by RCR.[24]

Lastly, but most importantly, almost all (8 of 9) Indigenous patients had PORT delay. Indigenous patients have lower 5-year survival rates (66% vs 41.5%) for HNSCC than non-indigenous people.[26] There has been no research to explore PORT delays in Aboriginal and Torres Strait Islander patients. However, a few studies have explored the reasons for poorer access to cancer treatment services in Indigenous Australians. Lyford *et al*.[27] and Anderson *et al*.[28] highlighted fear or lack of trust of mainstream health facilities, poor communication by healthcare providers, fatalistic beliefs about cancer, cultural insensitivity and lack of culturally relevant care, and difficulties navigating the health system as some reasons. Numerous interventions for improving accessibility to cancer treatment services have been suggested in the literature, focusing mainly on the following three domains: providing culturally appropriate and safe care (e.g. early involvement of Indigenous Health Workers and liaison officers and mandatory cultural awareness training for health workers), improving cancer knowledge in the Indigenous community (e.g. development of culturally appropriate educational resources) and cancer care coordination/navigation.[29,30]

The 42-day cut-off for commencement of PORT is based on retrospective studies[3,9,14] and a meta-analysis.[31] It is not likely that randomised studies will be conducted to establish an alternative metric other than

42 days. In addition to the ethical dilemma of conducting such studies, there is convincing evidence of inferior outcomes with delays in treatment. Studies have shown that rate of delay in PORT commencement can be reduced to <15%.[4,24] Therefore, this should be a metric for benchmarking for all facilities.

To achieve timeliness of PORT, facilities should track and manage process time periods. There has only been one study that has attempted to standardise care process time periods, although no consensus guidelines exist.[18] This study recommended surgery to PORT referral within 10 days, PORT referral to radiation oncology consult within 10 days, and radiation oncology consultation to PORT commencement within 21 days.[18] These timelines are achievable, however require effective communication and coordination of care within and between teams. The care process timeframes should be flexible in the event of delay in one or more steps of the care pathway. Surgical teams, particularly external facilities, should aim to complete referrals as soon as histopathology report is available and should involve the care coordinators at every step of the process. Indigenous and Torres Strait Islander patients should be appropriately supported, and Indigenous liaison officers/coordinators should be involved through all care processes.

Multidisciplinary teams meet weekly at TUH and the two external facilities. Improving communication and coordination of care by utilising existing electronic record platforms to generate electronic referrals at the first post-operative review in the head and neck multidisciplinary clinic, tracking patient progress through automated reminders to care coordinators and clinical teams and including a 'must treat by' option when booking radiation treatment are feasible and are being implemented at our institution. Educating the treating teams of the importance of timeliness of PORT, pre-operative radiation oncology consult when appropriate, patient education on the importance of compliance to PORT at initial consult,[15,32] pre-operative dental evaluations with intraoperative extractions,[33] compensation for unplanned radiation treatment prolongation and altered fractionation in those experiencing delays are other important considerations to ensure timely PORT.[21–24]

Limitations

The major limitation of this study is that it is a retrospective study with its inherent selection bias and unknown confounders. Exploring the reasons for treatment delays was limited by the data recorded in the electronic medical records and therefore could not have captured all possible reasons and granularity of decision making. Given the small number of patients in the no PORT delay group, it is possible that further factors associated with PORT delays were unable to be established in this study. Given this was conducted at a single institution in Australia, it may not be generalisable. However, international studies have demonstrated similar barriers to achieving timely PORT. The study did not evaluate impact of delays on treatment outcome given the small sample size. Additionally, multiple studies have sufficiently demonstrated the negative impact of treatment delays on outcomes.

Conclusion

In conclusion, this study demonstrates that the rate of PORT delay remains high despite strong evidence to suggest that these delays contribute to poor patient outcomes. Clinical teams should evaluate their processes and develop strategies for a sustainable model of well-coordinated care, taking into consideration that potential interventions will need to be tailored to address the specific geographical, socio-demographic and cultural factors. Organisations should strive to benchmark care processes times and evaluate at least annually. Further research exploring health worker and patient perspectives on the causes of PORT delay and potential targets of intervention are urgently needed. These studies should not only consider the efficacy of their proposed interventions but also the cost-effectiveness.

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Data availability statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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