Radiation cystitis in acute admissions for haematuria

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ABSTRACT

AIMS: To assess the outcomes of patients with haematuria from radiation cystitis admitted to Christchurch Hospital's Urology Service and identify treatment differences and hospitalisation trends.

METHODS: From November 2021 to January 2023, a retrospective analysis of 144 acute haematuria admissions was conducted. Data covered demographics, diagnosis, surgeries, complications and hospital stay length. Predictive factors for admissions and surgical interventions were explored.

RESULTS: Of the 144 admissions, 22 (15.3%) were diagnosed with radiation cystitis. The management strategies for radiation cystitis and non-radiation cystitis patients showed no significant differences in transfusion requirements, anti-bleeding medication usage (finasteride and/or tranexamic acid), or the need for acute or elective surgery. The average length of stay for admission was similar between the groups (radiation cystitis: 3.7 days, non-radiation cystitis: 3.5 days, $p<0.05$), but the readmission rate was significantly higher for radiation cystitis patients (59.1% vs 25.4%, $p<0.01$).

CONCLUSIONS: The management and hospital stay duration were similar for both cohorts; radiation cystitis patients faced increased readmissions, underscoring the necessity for rigorous monitoring and subsequent care. Upcoming research should target refining early interventions and management methods.

Haematuria is a common clinical presentation requiring acute admission to the hospital. It can be indicative of a variety of underlying urological conditions such as benign prostate hyperplasia, renal bleeding, cancer and radiation cystitis.[1,2] As a result of the ageing population, the incidence of haematuria-related acute admissions is rising, placing a growing burden on the healthcare system. Consequently, there is a growing need to optimise management pathways for patients presenting to hospital with haematuria.[3]

Radiation cystitis is a chronic inflammatory condition of the bladder that is recognised as a common late complication of radiation therapy for pelvic malignancies, including bladder, prostate and cervical cancer.[4–6] With the enhancement of cancer treatments and radiation therapy techniques resulting in an increasing number of cancer survivors, the prevalence of radiation cystitis has also grown. The pathophysiology of radiation cystitis is a complex cycle involving damage to the vasculature and smooth muscle cells of the bladder, resulting in ischaemia, subsequent fibrosis and ultimately impaired bladder function.[7]

Patients with radiation cystitis may present with various symptoms, including haematuria, clot retention, urinary urgency, frequency and dysuria.[4] The severity of haematuria in these patients can range from microscopic to life-threatening macroscopic haematuria in which hospitalisation is necessitated. In cases of severe haematuria, bleeding may be refractory to conservative management strategies; in these situations, invasive interventions such as endoscopic coagulation, embolisation or cystectomy may be necessitated.[4] Moreover, radiation cystitis and its associated symptoms can significantly impair a patient's quality of life through recurrent hospital admissions and ongoing interventions to manage these. The aim of the current study was to understand the patient outcomes of acute admissions to the Urology Service at Christchurch Hospital with haematuria caused by radiation cystitis.

Methods

Population

All patients acutely admitted to the Urology Service at Christchurch Hospital, New Zealand with haematuria between November 2021 to January 2023 were included in the study. Decision Support identified all acute admissions under Urology where the diagnosis was haematuria. Patients were excluded from analysis if trauma was listed as the primary cause of their presentation.

Data collection

The dataset was identified and a retrospective review of individual health records up to January 2023 was undertaken. Demographics, past medical history, final diagnosis, surgical procedures, medications, length of admission and readmission were extracted from the electronic health record Health Connect South (HCS). HCS is an Orion Health solution that collates information such as test results, medications, previous hospital admissions and emergency department attendances from disparate sources and presents it in a single patient view. The data were then entered into a de-identified database for statistical analyses.

Ethics

Ethics was obtained from the local district health board ethics approval committee; locality authorisation was obtained from the Te Whatu Ora – Waitaha Canterbury Research Office (RO #23122). This study was out of scope of the national New Zealand Health and Disability Ethics Committee (HDEC) ethics review.

Statistics

The statistical comparisons of the different management approaches between the presentations with radiation cystitis vs non-radiation cystitis haematuria were undertaken using Chi-squared tests or Fisher's exact tests when the minimum expected frequencies were <5.0. The length of hospital stay was compared using the Mann–Whitney U test and the percent of admissions requiring a readmission was compared using a Chi-squared test.

Results

Case identification

A total of 99 patients who were acutely admitted to the Christchurch Urology Service for haematuria were identified by Decision Support. There were 145 admissions in total (including patient representations). Of these one was excluded, as the primary cause of their haematuria was acute trauma to the bladder. Data were extracted from the remaining 144 presentations for analysis.

Patient demographics and clinical characteristics

Table 1 outlines the demographic data of the population who were admitted under the Christchurch Urology Service with an acute presentation of haematuria. There were 98 patients (96% male). The median age at presentation was 77 years (range: 28–96).

All patients were investigated for a cause of haematuria using our standard investigation pathway, which involved CT IVU or renal ultrasound and flexible cystoscopy. Where no clear cause of haematuria was evident, the cause was determined as "unknown". It is expected that for many of the male patients in this group, benign prostatic bleeding will have been the most likely aetiology. All the patients had a cystoscopy to confirm the diagnosis of radiation cystitis and to rule out secondary malignancy.

Details of radiation therapy administered

Table 2 provides an overview of the radiation therapy details. The majority of patients received radiation for prostate cancer (N=20).

Management of radiation cystitis

Table 3 summarises the distribution of management approaches for each group (radiation cystitis versus non-radiation cystitis), along with the associated p-values.

There is no significant difference between the radiation cystitis and non-radiation cystitis groups in terms of patients requiring transfusion (p=0.2), starting on finasteride and/or tranexamic acid medication (p=0.4), undergoing acute surgery (p=0.9), or undergoing elective surgery (p=0.7) (Table 3). A significant difference was observed in the use of hyperbaric oxygen therapy (HBO), with 54.5% of patients in the radiation cystitis group receiving this treatment compared to only 3.3% in the non-radiation cystitis group (p <0.0016).

Hospital stay and readmissions

The table below summarises the average length of stay, readmission rates and associated p-values for each group.

There was no significant difference in the average length of stay for admission between the radiation cystitis group (3.7 days; range: 1–11) and the non-radiation cystitis group (3.5 days; range: 1–17) (p >0.05) (Table 4). However, a significant difference was observed in the readmission rate, with 59.1% of patients in the radiation cystitis group experiencing readmissions compared to only 25.4% in the non-radiation cystitis group (p=0.0016). The median time between a patient receiving radiation treatment and presenting with radiation cystitis-induced haematuria was 7 years (range: 0.2–14 years).

Figure 1: An overview of included and excluded patients who had an acute admission for haematuria.

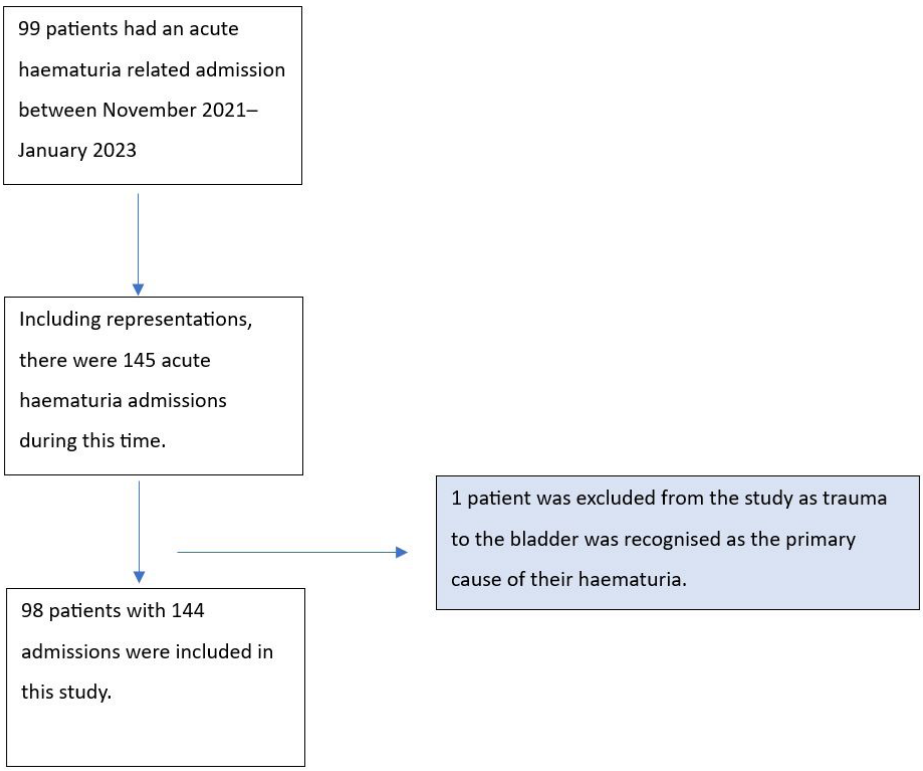

Table 1: Patient demographic data.

Demographics	**n (%)**
Total number of patients	98
Total number of admissions	144
Gender (male)	94 (96%)
Ethnicity	
NZ European	61 (61.6)
NZ Māori	5 (5.1)
Chinese	2 (2.0)
Samoan	1 (1.0)
Other	30 (30.3)
Median age at diagnosis (years)	77 (range: 28–96)
Final diagnosis	
Unknown	31 (21.5%)
Radiation cystitis	22 (15.3%)

Table 1 (continued): Patient demographic data.

Bladder malignancy	15 (10.4%)
Post-operative complication	14 (9.7%)
Vascular prostate	15 (10.4%)
Trauma related to catheter	13 (9.0%)
Renal malignancy	7 (4.9%)
Anticoagulant use	5 (3.5%)
Prostate cancer	6 (4.2%)
Secondary to UTI	6 (4.2%)
Not investigated at patient request	4 (2.8%)
Bladder calculi	3 (2.1%)
ESWL	1 (0.7%)
Ureteric stone	1 (0.7%)
Bladder invasion of uterine cancer	1 (0.7%)

* The classification of "Other" as the patient's ethnicity was sourced directly from the Health Connect South portal. It represents the primary ethnicity chosen by the patient at some point in time.

Table 2: Breakdown of radiation components and indications.

Overview of radiation treatment	**N (%)**
Indication	
Prostate cancer	20 (90)
Bladder cancer	1 (5)
Precursor T-cell ALL	1 (5)
Type of radiation	
Short-course	2 (9)
Long-course	15 (68)
Information not available	5 (23)
Length of radiation (mean, days)	49.8 (range: 2–58)

Table 3: Management of patients with radiation cystitis vs non-radiation cystitis haematuria.

Management	Radiation cystitis n (%)	Non-radiation cystitis n (%)	p-value
Transfusion required	6 (28.6)	20 (16)	0.2
Started on antibleeding medication (finasteride and/or tranexamic acid)	4 (19.0)	38 (30.6)	0.4
Underwent acute surgery	3 (14.3)	15 (12.1)	0.9
Underwent elective surgery	1 (4.8)	13 (10.5)	0.7
Hyperbaric oxygen therapy	12 (54.5)	4 (3.3)	0.0016

Table 4: Hospital stay and readmissions for patients with radiation and non-radiation cystitis.

Measure	Radiation cystitis	Non-radiation cystitis	p-value
Average length of stay for admission	3.7 (range: 1–11)	3.5 (range: 1–17)	>0.05
Number of readmissions	13 (62.0%)	31 (25.0%)	<0.01

Discussion

Radiation cystitis is a well-recognised complication of radiotherapy to the pelvis and a significant cause of haematuria admissions to hospital. As a result of increasing usage of radiotherapy in the management of pelvic malignancies (especially in prostate cancer), understanding the management pathways, hospital stays and readmission rates for radiation cystitis patients is critical in optimising patient quality of life and improving outcomes. Our findings revealed no significant differences in management strategies, but a significantly higher readmission rate among radiation cystitis patients compared to non-radiation cystitis patients indicated this complication represents a significant burden of care to the health system.

The management of radiation cystitis-induced haematuria often requires a tailored approach to optimise patient outcomes and can include a variety of treatment modalities. Strategies tend to focus on conservative measures including irrigation of the bladder, sufficient analgesia and the use of anticholinergics.[3] We found no statistically significant differences in terms of patients requiring transfusion (although this group are twice as likely to require a transfusion), commencement of anti-bleeding medication (such as tranexamic acid) or undergoing acute or elective surgery. Higher rates of transfusion and surgical intervention in radiation cystitis are markers of the more severe and refractory nature of the underlying condition, which can often result in prolonged and often more severe bleeding.[8] However, there is limited research surrounding the management differences and further investigations are required to substantiate our observations to delineate the treatment strategies among these patients.

HBO is recognised as an important treatment in radiation-induced haematuria, as it mitigates bleeding through the promotion of angiogenesis, tissue healing and anti-inflammatory processes.[9,10] Additionally, the utilisation of HBO in these patients has been shown to improve quality of life and reduce the likelihood of subsequent invasive interventions in patients with radiation cystitis.[9,10] In a study by Pereira et al. (2020), while they found a 92.4% success rate in the control of haematuria, 24.7% of patients presented with recurrence of haematuria within a 63 month follow-up period.[11] Similar rates of recurrence have also been found in other studies.[12–14] As a proportion of readmitted patients had previously received HBO treatment, it raises questions surrounding the efficacy of the treatment and the criteria in which patients have been selected. It is possible that some patients may not be experiencing long-lasting benefits from HBO and may require more intensive or extended sessions. Alternatively, a patient's underlying comorbidities or lifestyle factors, including smoking and drinking,

could influence treatment outcomes.[15] Bouaziz et al. (2016) and Mougin et al. (2016) demonstrated that anticoagulant therapy was a significant negative predictive factor in the success of HBO therapy.[16,17] Further research is required to better understand the complex interplay between patient characteristics, severity of radiation cystitis and the nuances of HBO.

The length of stay for hospital admissions for patients presenting with haematuria is influenced by numerous factors, including the underlying diagnosis, severity of haematuria and the availability and effectiveness of treatment. Prolonged admission to hospital can negatively affect patient quality of life and outcomes; therefore, understanding the differences in duration of hospital stay for different underlying conditions is critical in optimising care. In our study, we found no significant difference in the average length of stay for admission between the radiation cystitis group (3.5 days; range: 1–11) and the non-radiation cystitis group (3.7 days; range: 1–17) ($p > 0.05$). However, it is essential to consider the influence that risk factors such as patient comorbidities, age and severity of the condition causing the haematuria may have on individual length of stay. Furthermore, additional investigations are required to explore the impact that early intervention and more intensive management have on altering the length of hospital stay. Although the average length of stay for admission did not differ significantly between the two groups, the readmission rate was substantially higher for radiation cystitis patients (62.0% vs 25.0%, $p=0.0003$). The increased rate of readmission in patients with radiation cystitis may be attributed to the recurrent and persistent nature of the underlying condition,[4] which can often be more challenging than non-radiation cystitis-induced haematuria to manage. Sanguedolce et al. (2021) examined patients with radiation-induced haematuria to pinpoint those at an elevated risk of hospital admission and invasive treatment. Their findings revealed a significant association between anticoagulant/antiplatelet therapy and salvage radiotherapy with a higher likelihood of hospitalisation.[18] These results highlight the need for closer clinical monitoring and follow-up care in patients with radiation cystitis to reduce the risk of acute admission to hospital and improve patient outcomes.

The median length of time between radiation treatment being delivered and first presentation with radiation cystitis was 7 years. This is similar to previous studies looking at HBO therapy.[12] It is anticipated that patients have often fallen out of regular oncology follow-up by this timeframe, and the long-term development of radiation cystitis must be considered a survivorship issue in patients undergoing this treatment. Appropriate patient counselling is recommended prior to radiation treatment to ensure that the potential long-term risks are clearly articulated, to inform patient decision-making.

The limitations of this study include its retrospective design and the relatively small sample size, which could affect the generalisability of the findings. Additionally, the study did not analyse potential confounding factors, such as comorbidities that may have influenced the management strategies and readmission rates. Moreover, the emergency department presentations and subsequent non-admissions represent a potential gap in our data. Some presentations that did not require admission under the Urology department may still have resulted in significant medical interventions or referrals. Future research should focus on larger, prospective studies or randomised controlled trials to further elucidate the differences in management strategies and readmission rates between radiation and non-radiation cystitis patients.

Conclusion

Radiation cystitis creates a significant burden on patients and the healthcare system. The complexities associated with radiation treatment and the difficult to manage long-term sequalae warrants consideration as part of the treatment decision to offer radiation to patients, particularly in conditions where the long-term benefit from a cancer-control perspective may be modest, or where valid alternatives exist. The findings of this study advocate for further research into effective management strategies and interventions to mitigate the burden of radiation cystitis.

COMPETING INTERESTS
There are no conflicts of interest to declare. This project was funded by the Canterbury Urology Research Trust.

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