



ORIGINAL RESEARCH ARTICLE

Lower proportion of bladder cancer diagnosed at unscheduled hospitalization after introduction of standardized care pathways in Sweden

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ABSTRACT

Objective: To investigate the probability for being diagnosed with bladder cancer in conjunction with unscheduled hospitalization before and after 2015 when standardized care pathways (SCP) for urinary tract cancer was introduced in Sweden.

Material and methods: Unscheduled hospitalization was defined as in-hospital care with transurethral resection of bladder tumor without previous outpatient cystoscopy in patients with bladder cancer in BladderBaSe 2.0. Three calendar years before introduction of SCP (2011–2014) and after (2016–2019) were compared using adjusted logistic regression models to calculate the odds ratio (OR) for being diagnosed at an unscheduled hospital admission.

Results: The study included 9998 and 11,647 patients diagnosed before and after the introduction of SCP, respectively. Proportions of patients diagnosed with bladder cancer in conjunction with unscheduled hospitalization was 13% before and 7% after implementation of SCP. Compared to patients diagnosed prior to introduction of SCP, patients diagnosed after had an adjusted OR for unscheduled hospitalization of 0.50 (95% confidence interval 0.46–0.55).

Conclusions: Following the implementing SCP for bladder cancer, the proportion of patients diagnosed with bladder cancer during an unscheduled hospitalization in Sweden decreased, even after adjustment for potential confounders.

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Introduction

Three out of four patients diagnosed with bladder cancer present with macroscopic hematuria, also in population-based contemporary Swedish data [1], which has the highest positive predictive value for cancer out of all isolated alarm symptoms, although with variation of risk estimates related to the characteristics of the investigated population [2, 3]. A Swedish national healthcare initiative with standardized care pathway referral (SCP) for urinary tract cancer was launched in September 2015 for five malignancies including bladder cancer, aiming to reduce lead times, improve timely cancer diagnosis and treatment and increase patient satisfaction. In brief, SCP for urinary tract cancer include patients with suspicion of urothelial carcinoma in the urinary tract with either macroscopic hematuria in individuals

50 years of age and above or radiologic or endoscopic findings suggesting urothelial carcinoma. Patients are referred to a computed tomography urography (CTU) and subsequent cystoscopy, with a target lead time from referral to transurethral resection of bladder tumor (TURB) of 18 days for patients diagnosed with bladder cancer.

The introduction of SCP not only defined for the first time target lead times for CTU and urology referral with cystoscopy, but also specified lead times from referral to TURB. After the introduction of SCP, the median time from referral to TURB decreased from 37 to 27 days in Sweden [4].

Emergency presentation varies among different cancers and in a population-based study from UK 19% of all bladder cancer patients were diagnosed at unscheduled emergency

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hospitalization [5], where being female and having lower socioeconomic status were associated with greater risk of such diagnostic presentation. A recent study from a Swedish county hospital reported that patients diagnosed with bladder cancer at unscheduled admission decreased from 15 to 10% after the introduction of SCP [1].

The aim of this study was to investigate the introduction of SCP as a national healthcare policy by comparing calendar time periods and assessing association with bladder cancer diagnosis at unscheduled hospitalization admission, using the population-based nationwide research database (BladderBaSe 2.0) [6].

Methods

Study population selection

Patients diagnosed with bladder cancer 2011–2014 and 2016–2019 in BladderBaSe 2.0 were included in the study. The calendar time categories were selected to reflect the era before and after the implementation of SCP in 2015.

Variables

BladderBaSe 2.0 is a bladder cancer research database linking data from the Swedish National Register for Urinary Bladder Cancer (SNRUBC) to national healthcare and demographic registers [6]. This study utilized information about age, sex, clinical TNM (tumor/node/metastasis) at diagnosis, grade (WHO 1999), and number of days from referral to TURB. Highest educational level (in three categories (mandatory school/high school/university)) as a proxy for socioeconomic status and drug comorbidity index (DCI) as a measure of comorbidity [7] were obtained from demographic databases and the patient register. To adjust for use of anticoagulants, possibly related to propensity to develop macroscopic hematuria facilitating bladder cancer evaluation [8] and timely bladder cancer diagnosis [9], such prescription was assessed from the Drug Prescription Register (DPR) that is linked to BladderBaSe 2.0. Prescription of anatomical therapeutic chemical (ATC) codes for anticoagulants (B01) within 12 months of bladder cancer diagnosis was stratified as platelet aggregation-inhibitors (B01AC) versus all other B01-codes including coumarin-derivates and new oral anticoagulants.

For patients diagnosed in 2016–2019, SNRUBC included a variable indicating whether or not SCP-referral was applied for each individual patient. The SCP-referral variable is a checkbox, which is ticked if the patient was subjected to such referral, and this could be ticked at any time in time of the patient care chain.

Unscheduled admission and hospitalization was defined by in-hospital care together with a procedure code for TURB (KCD02) within 1 week before date of bladder cancer diagnosis in the SNRUBC combined with absence of a procedure code for cystoscopy (UKC02) in outpatient care within 12 months prior date of bladder cancer diagnosis. This captures all unplanned in-hospital admissions where a new bladder cancer diagnosis

was made during the same in-hospital admission and without prior outpatient cystoscopy. The 1-week window was chosen to allow for discrepancies in date of bladder cancer diagnosis in the SNRUBC and the dates of hospitalization in the in-hospital register. Thus, if the patient was discharged with a new bladder cancer diagnosis without having a TURB performed during that hospitalization, it was not considered as an event.

Statistical analysis

Baseline characteristics were displayed descriptively in calendar time categories for patients diagnosed before and after the introduction of SCP. The proportion of patients diagnosed through unscheduled admission were graphically shown stratified for calendar year, and displayed stratified for sex, age, educational level, DCI (in tertiles) and use of anticoagulants. Association between introduction of SCP and unscheduled hospitalization for bladder cancer was estimated using odds ratios (OR) based on logistic regression. The model was adjusted for age (continuous), sex, DCI (stratified in tertiles), educational level, and use of anticoagulation. Subgroup analyses were performed in men and women separately. A separate descriptive sensitivity analysis was performed using individuals subjected to SCP-referral, where the proportion of patients diagnosed through unscheduled admission were stratified for calendar year. For all statistical analyses the R statistical package version 4.1.1 was used.

Ethics approval

The Research Ethics Board at Uppsala University, Sweden approved this study (year of approval and diary number: 2015-277, 2019-03574, 2020-05123, and 2022-01747-02).

Results

The study included 9998 patients diagnosed before and 11,647 patients after the introduction of SCP with patient and tumor characteristics presented in Table 1. Median number of days from referral to bladder diagnosis decreased from 39 (inter quartile range [IQR] 23–61) days before to 27 (IQR 16–42) days after implementation of SCP, and the use of any type of anticoagulants decreased from 4462 (45%) to 4501 (39%). After SCP introduction 71% of all patients diagnosed with bladder cancer were subjected to SCP-referral (Table 1).

The proportion of bladder cancer patients diagnosed at unscheduled hospital admission was 13% before and 7% after the introduction of SCP. Annual proportions diagnosed at unscheduled hospital admission are given in Figure 1. Proportions stratified by sex, age, educational level, DCI, use of anticoagulants, and healthcare region both before and after SCP introduction are shown in Supplemental Table 1. Higher age, lower educational level, higher DCI had higher proportions of patients diagnosed at unscheduled hospital admission. The proportion unscheduled hospital admission in the six healthcare

Table 1. Patient and tumor characteristics stratified before and after implementation of standardized care pathways.

Patient and tumor characteristics	Before SCP introduction (2011–2014, <i>n</i> = 9998) numbers (%)	After SCP introduction (2016–2019, <i>n</i> = 11,647) numbers (%)
Median number of days from referral to TURB (IQR)	39 (23–61)	27 (16–42)
Median age at diagnosis (IQR) years [^]	73 (66–80)	74 (67–80)
Male	7501 (75)	8658 (74)
Female	2497 (25)	2989 (26)
DCI (tertiles)		
–0.75	3449 (35)	4106 (35)
0.75–2	3017 (30)	3440 (30)
2–	3532 (35)	4101 (35)
Educational level*		
Low	3981 (40)	4011 (35)
Middle	3888 (39)	4868 (42)
High	1989 (20)	2600 (23)
Clinical tumor stage		
Ta/Tx	5196 (52)	6084 (52)
CIS	275 (3)	325 (3)
T1	2316 (23)	2751 (24)
T2–T4	2211 (22)	2487 (21)
Clinical nodal stage		
N0/Nx	9702 (97)	11,265 (97)
N1–N3	296 (3)	382 (3)
M-stage		
M0/Mx	9689 (97)	11,251 (97)
M1	309 (3)	396 (3)
Grade (WHO 1999)		
Gx	423 (4)	396 (3)
LMP	213 (2)	194 (2)
G1	2451 (25)	2536 (22)
G2	2925 (29)	3422 (29)
G3	3986 (40)	5099 (44)
Anticoagulants at diagnosis		
No	5536 (55)	7146 (61)
Platelet aggregation-inhibitors	3169 (32)	3284 (28)
Other	1293 (13)	1217 (10)
SCP referral		
No/missing	N/A	3328 (29)
Yes	N/A	8319 (71)

IQR: inter quartile range; DCI: Drug Comorbidity Index; SCP: standardized care pathways; CIS: Carcinoma *in situ*; TURB: transurethral resection of bladder tumor. [^]Missing value 14 individuals; *Missing data for 140 and 168 individuals, respectively.

regions in Sweden ranged between 8 and 19% prior to and 3–9% after the introduction of SCR, respectively. All strata, except women 90 years of age and above, had lower proportions of unscheduled admissions with bladder cancer diagnosis after the implementation of SCP, as compared to before.

In a logistic regression model the OR for year of bladder cancer diagnosis after introduction of SCP as compared to before for being diagnosed with bladder cancer through unscheduled emergency hospital admission was 0.50 (95% confidence interval [CI] 0.46–0.55). Similar risk estimates were observed in subgroups of men and women (OR 0.54 (95% CI 0.44–0.65) and OR 0.50 (95% CI 0.44–0.55), respectively) (Table 2).

In a descriptive sensitivity analysis considering only those 8319 individuals referred through SCP, the proportion diagnosed

at unscheduled hospital admission was 5%, with annual proportions is shown in Supplemental Figure 1.

Discussion

Since the introduction of SCP for bladder cancer in Sweden in 2015, the proportion of patients being diagnosed in conjunction with unscheduled hospital admission declined from 13 to 7%. After adjustment for age, sex, comorbidity, educational level, and anticoagulant use, the introduction of SCP remained significantly associated with a reduced occurrence of unscheduled hospital admission (OR 0.50).

Study strengths include the large cohort and the nationwide, population-based study design entailing coverage of hospital and outpatient services. Furthermore, SNRUBC has high

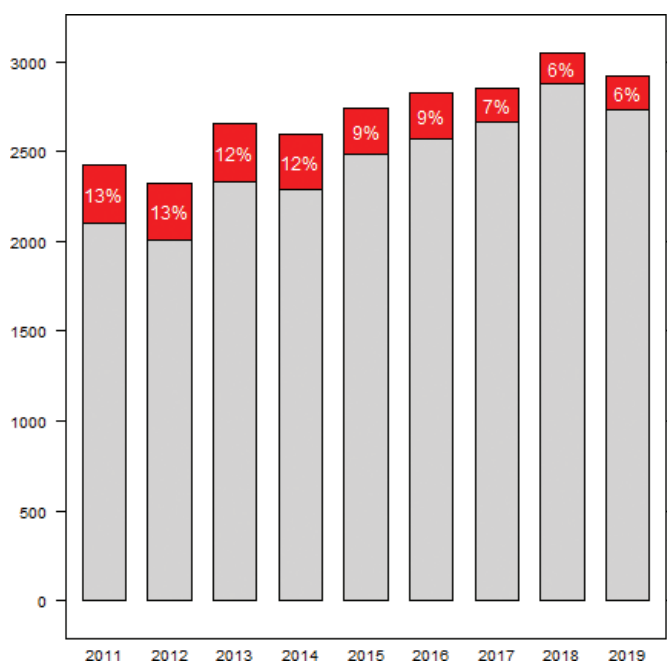


Figure 1. Annual numbers and proportions diagnosed with bladder cancer at unscheduled hospitalization throughout the study.

coverage and validity of the included variables [6], and the patient register data included to capture the outcome has a high accuracy for surgical procedures [10]. The use of BladderBaSe 2.0 also enabled adjustment for covariates associated with time trends in bladder cancer epidemiology in Sweden over the studied period. For example, bladder cancer incidence has increased in Sweden during later years, especially in older men [11].

A limitation is that changes in the population and care patterns during the study period other than those tied to age, sex, comorbidity, educational level, and use of anticoagulants could not be adjusted for. Firstly, SCP itself might increase the possibility that patients with obvious bladder cancer findings at CTU were directly scheduled for TURB without outpatient cystoscopy [12] and thus fulfilling the applied study definition of unscheduled hospitalization. However, such misclassification would increase the proportion of individuals diagnosed by unscheduled hospital admission biasing the results toward null. Secondly, changes in care patterns may have occurred following the decreasing number of in-hospital beds over calendar time [13], which may have decreased the propensity for physicians in emergence care to subject patients with, for example, macroscopic haematuria to unscheduled hospital admission. The uptake of SCP depends on patient characteristics and

structural factors, which both vary between healthcare regions. On an individual patient basis, we lack information on whether one or both of these factors determined if SCP was applied or not. Hence, to disentangle regional differences in uptake of SCP was not possible.

Our results are in line with a previous study from United Kingdom (UK) where older and individuals with higher deprivation index had higher proportions of bladder cancer emergency presentation [5]. The higher proportions of unscheduled hospital admissions by age and comorbidity in this study are also in line with a previous report on patients hospitalized for macroscopic hematuria: an audit from UK reported a median age of 78 years and a median American Society of Anaesthesiologists (ASA) score of 3 were reported among those patients hospitalized for macroscopic hematuria [14]. On the other hand, except among women older than 90 years of age, the proportions unscheduled hospital admission at bladder cancer diagnosis were similar between males and females in this study, contrasting a greater risk in females reported from UK [5].

Differences in referral recommendations might be one explanation for divergent findings regarding gender-specific risks of unscheduled hospital admission at bladder cancer diagnosis in this study [5]. The UK National Institute for Health and Care Excellence (NICE) recommends referral for individuals aged over 45 years with either unexplained visible hematuria without urinary tract infection (UTI) or persistent or recurring visible hematuria after UTI-treatment [15]. In Sweden, SCP criteria include patients above 50 years of age irrespective of UTI-related symptoms or not [16], despite retrospective data suggesting that the risk of bladder cancer in this subgroup is approximately 50% lower [17], caused by the high incidence UTI with hemorrhagic cystitis in females [18]. However, the Swedish referral recommendation is supported by an increased risk of being diagnosed with more advanced bladder cancer after treatment related to UTI [19]. Additionally, Sweden has abandoned testing for asymptomatic microscopic hematuria since many years in contrast to NICE guidelines, which recommend referral of individuals aged over 60 with unexplained non-visible hematuria [20]. Consequently, an increased awareness among clinicians about macroscopic hematuria as an important alarm symptom for urinary tract cancer caused by the introduction of SCP might have improved diagnostic practices and contributed to the decrease in unscheduled hospital admission at bladder cancer diagnosis.

Although we have no information on the specific reason for unscheduled hospital admission, be it hematuria, pain, sepsis, renal failure or social restrictions, macroscopic hematuria is the

Table 2. Multivariable logistic regression model for year of bladder cancer diagnosis after introduction of SCP as compared to before and the odds ratios for bladder cancer diagnosis through emergency admission, adjusted for by age (continuous), comorbidity (DCI = Drug Comorbidity Index), educational level, and use of anticoagulants, in full study population and in subgroups of men and women.

Patient and tumor characteristics	Full population	Subgroup of men	Subgroup of women
Year of bladder cancer diagnosis	Adjusted odds ratio (95% confidence interval)		
Before SCP introduction (2011–2014)	1	1	1
After SCP introduction (2016–2019)	0.50 (0.46–0.55)	0.50 (0.44–0.55)	0.54 (0.44–0.65)

SCP: standardized care pathways.

most likely candidate [1, 21]. Moreover, visible hematuria is responsible for one out of five urological emergencies in a tertiary care setting [22]. A reduction in unscheduled hospitalization at bladder cancer diagnosis might increase the likelihood of the TURB being performed in an elective setting by an experienced urologist and hence decrease hospital stay and improve recurrence-free survival [23]. Other benefits follow the introduction of SCP. In qualitative research patients subjected to SCP identified one-stop policy as beneficial [24]. Prior to SCP implementation for urinary tract cancer in Sweden, fast-track urological cancer assessment for patients with macroscopic hematuria was beneficial from a cost-effectiveness perspective [25]. Moreover, a lower proportion of muscle-invasive bladder cancer following SCP implementation has been reported [26]. Whether this decreased proportion muscle-invasive bladder cancer after implementation has contributed to an observed decrease in age-standardized mortality is not possible disentangle [27].

Conclusions

After national implementation of SCP for bladder cancer in Sweden, a clinically relevant lower proportion of patients was diagnosed during unscheduled hospital admissions. Our results indicate meaningfully improved diagnostic pathways for bladder cancer following the introducing general guidelines with target lead times for diagnostic actions.

Competing interests

None for any of the authors, i.e., the authors report no conflicts of interest.

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