Non-muscle invasive bladder cancer: Are epicrises the ‘Bermuda Triangle’ of information transfer?

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Introduction
The aim of the study was to collect information regarding the quality of communication of risk-determining factors or risk profile, and the guideline conformity of recommendations for adjuvant treatment in patients with non-muscle invasive bladder cancer (NMIBC) between clinical and ambulatory urologists.

Material and methods
At three German urological clinics during the period between 2012-2014, epicrises of 1,033 NMIBC-patients were retrospectively summarised to 505 tumour episodes (tumour resection including any re-resections) and analysed regarding the endpoints 1) risk profile is explicitly named or recorded risk factors are sufficient for the determination of risk profile, and 2) guideline conformity of treatment recommendation. Independent factors influencing the endpoints were determined by means of multivariate logistic regression models.

Results
The risk profile was explicitly named for 3.6% of tumour episodes; for 68.9% a risk profile could be derived from the information in the epicrises. Treatment recommendations were given for 93.7% of tumour episodes, but only 17.8% were guideline compliant. 42.6% of the recommendations were not reliably effective; 33.1% and 0.2% resulted in under- and overtreatment respectively. Neither endpoint showed gender specific or regional differences, but both were considerably less likely to be achieved in case of recurrence.

Conclusions
The discrepancy between treatment recommendation (93.7%) and guideline compliance (17.8%) could indicate a lack of familiarity with guidelines. The quality of the epicrises of NMIBC-patients was poor and bore the potential risk of undertreatment. The results of this study are not necessarily applicable to other clinics, but could, however, prompt physicians to re-examine epicrises for the fulfillment of the quality criteria examined here.
to non-muscle invasive bladder cancer NMIBC) [5]. The recurrence risk for NMIBC is affected by tumorigenic criteria including previous recurrence rate, focality and tumour size; grading, infiltration depth and a (concomitant) carcinoma in situ (CIS) moreover correlate with the progression probability [6]. Following primary NMIBC treatment with transurethral resection and, possibly, immediate post-operative intravesical instillation of chemotherapy and second resection, NMIBC-patients should undergo a risk stratification on the basis of the aforementioned tumorigenic criteria for low, intermediate and high-risk pursuant to European Association of Urology (EAU) guidelines [7–10]. Depending on the risk group, the probability of recurrence or progression within 5 years is 31–78%, or 0.8–45%, respectively [6]. In long-term follow-up, up to 54% of patients with high-risk NMIBC develop muscle invasive bladder cancer with a cancer-specific survival of only 32% [11].

The aim of risk-adapted adjuvant treatment is therefore to prevent or at least delay tumour recurrence or progression, whereby numerous studies confirm the guideline adherence to be poor [12–17]. Based on data from 4,545 high-risk NMIBC-patients taken from the Surveillance, Epidemiology and End-Results (SEER)-Database, Chamie et al. showed that physician-related factors – particularly regarding recommended follow-up examinations, as well as the recommendation and application of risk-adapted intravesical installation treatments – contributed considerably more to poor guideline adherence than patient- or tumour-related factors [13].

A study by Gontero et al. on 344 NMIBC-patients in eight Italian referral centres showed the following information to be readily available to ambulatory-urologists: Recurrence status 100%, focality 98.8%, tumour size 87.2%, infiltration depth (incl. CIS) 99.2%, WHO-grading (1973) 100%, WHO-grading (2004) 100%, risk-group 100% [18]. The basis of rational and guideline-compliant treatment is the communication of just these risk factors or at least the respective appropriate risk profile from the clinic to the ambulatory urologist. In Germany there is deficient information on the quality of such information transfer from the clinic to doctor's office. In a previous study by our group, although 91% of the clinic urologists questioned rated the risk profile as an essential or important part of the discharge letter, its inclusion was only confirmed by 24% of the ambulatory urologists questioned [19]. Although 62% of the clinical urologists in the study believed the recommendation for risk-adapted adjuvant treatment was included in the discharge letter, this was confirmed by only 20% of the ambulatory urologists questioned. Generally speaking, there were clear indications that clinical urologists overrated the quality of discharge letters.

**Topic of investigation**

The aim of this study was to objectify the quality of discharge letters provided by selected urological clinics in Germany for NMIBC-patients regarding the following endpoints:
1) Risk profile is explicitly named or the recorded risk factors are sufficient for the determination of the risk profile and
2) Treatment recommendation is guideline compliant vs. not or not reliably guideline compliant or non-existent.

**MATERIAL AND METHODS**

**Patient selection and study criteria**

A retrospective study based on surgical operation documentation and discharge letters from the Department of Urology at Magdeburg University Hospital, Ruppin Clinics in Neuruppin and St. Elisabeth Hospital Straubing between 2012 and 2014 identified all cases with the operation codes 5-573.40 or 5-573.41 (transurethral resection of the bladder, with or without hexaminolevulinic acid) in which the diagnosis NMIBC was given in the discharge letter. Thus for a total of 1,033 cases, the patient identifiers, dates of surgery and surgical procedures, the risk-determining factors infiltration depths including the presence of a concomitant CIS, grading (WHO 1973 and 2004), recurrence status, tumour size and focality, as well as the specific risk profile documented in the epicries were recorded in a database. It was also recorded whether – and if so, which – adjuvant treatment was recommended in the discharge letter. Excluded were:
- double entries (n = 10),
- tumour-free follow-up cystoscopies without resection (n = 23),
- inconsistent data, e.g. details of a tumour-free follow-up re-resection together with details of grading or infiltration depth for the same case (n = 3),
- at the beginning of the recording period, patients with second resection and initial resection performed prior to 01.01.2012 (n = 60),
- at the end of the recording period, patients with initial resection and second resection after 31.12.2014 (n = 32).

After consideration of the exclusion criteria, a total of 905 cases were collated to tumour episodes. A tumour episode comprises the initial transure-
The completeness of risk determining parameters, specifying of the risk profile, as well as the distribution of treatment recommendations and their guideline conformity ordered according to risk profile, study centre and year of operation were described. Two multivariate logistic regression models (MLRM) were applied to determine the independent factors affecting the binary endpoints 1) Risk profile is explicitly named or the recorded risk factors are sufficient for the determination of the risk profile (MLRM 1) and 2) treatment recommendation is guideline compliant vs. not or not reliably guideline compliant or non-existent (MLRM 2).

In addition to the patient's age (continuous) and gender (male, female), treating clinic (clinic 1, 2 or 3) and year of surgery (2012, 2013, 2014), all risk-determining parameters available in >90% of all tumour episodes were integrated in the MLRM: infiltration depth (pTa vs. CIS, pT1 and pTa-1 with CIS), WHO-grading 1973 (G1, G2, G3) and recurrence status (primary vs. recurrent tumour).

Infiltration depth and WHO-grading were excluded from the MLRM 1, as both factors alone could suffice to define the risk profile: pT1 or CIS or G3 are to be classed as high. The 1973 WHO-grading was excluded from MLRM 2 due to its strong collinearity with infiltration depth. The effect of the examined criteria on the endpoints was described by means of the odds ratio (OR) and its 95%-confidence-interval (CI); p-values were always bilateral. A p-value <0.05 was determined as a statistically significant result. Data analysis was performed by means of SPSS 23 (IBM Corporation 2015, Armonk, NY, USA).

RESULTS

Clinic 1, clinic 2 and clinic 3 contributed 160, 140 and 205 tumour episodes respectively. There were 185, 173 and 147 tumour episodes respectively in 2012, 2013 and 2014. A specific risk profile was given for 3.6% (18/505) of tumour episodes. Details of risk-determining parameters based on the epicri ses were available as follows: infiltration depth incl. presence of a concomitant CIS 96.4% (487/505), WHO-grading 1973 92.5% (467/505), WHO-grading 2004 62.2% (314/505), recurrence status 99.4% (502/505, 326 primary tumours and 176 recurrent tumours), focality 76.0% (384/505) and tumour size 23.8% (120/505).

It was possible to derive a risk profile from the medical and histopathological data in the epicri ses for 68.9% (348/505) of tumour episodes: in 3.2% (16/505), 36.8% (186/505) and 28.9% (146/505) there was...
was a low, intermediate and high risk respectively. Between 2012 and 2014 the percentage of epicrises with adequate data for a risk profile increased from 62.7% to 74.8%.

In the multivariate analysis, the probability for an explicitly named risk profile or adequate information to define a risk profile (MLRM 1) was not gender-specifically distributed (p = 0.171) and there was no significant difference (p = 0.476) between clinics. It increased with each year of life by 2.8% (OR 1.028; 95%-CI 1.016–1.040; p < 0.001) and between 2012 and 2014 by factor 2.3 (OR 2.304; 95%-CI 1.392–3.813; p = 0.001). Compared to a primary tumour, the probability in the case of recurrence dropped by 73.6% (OR 0.264; 95%-CI 0.175–0.397; p < 0.001).

A treatment recommendation was given for 93.7% (473/505) of tumour episodes – irrespective of guideline conformity. The percentage of epicrises with a treatment recommendation increased from 90.3% in 2012 to 95.9% in 2014. The figures for treatment recommendations in the categories not reliably effective, undertreatment and overtreatment were 42.6% (215/505), 33.1% (167/505) and 0.2% (1/505), respectively. Treatment recommendations were guideline-compliant for 17.8% (90/505) of tumour episodes.

Table 1 shows the distribution of individual treatment recommendations and guideline conformity according to risk profile, clinic and year. Multivariate analysis showed the probability of a guideline compliant treatment recommendation (MLRM 2) to be evenly distributed between genders (p = 0.945), there was no significant difference between clinics (p = 0.060). It decreased with each year of life by 3.4% (OR 0.996; 95%-CI 0.951–0.983; p < 0.001), between 2012 and 2014 by 53% (OR 0.47; 95%-CI 0.245–0.900; p = 0.023) and was 60.2% lower for a recurrent than for a primary tumour (OR 0.398; 95%-CI 0.225–0.703; p = 0.002). For infiltration depths CIS, pT1 and pTa-1 with accompanying CIS, the probability increased compared to pTa by factor 6.3 (OR 6.296; 95%-CI 3.663–10.820; p < 0.001).

**DISCUSSION**

As far as we know, no other study has addressed the issue of the quality of the information on risk stratification and the guideline conformity of recommendations for adjuvant treatment in discharge letters for patients with NMIBC. The quality of the epicrises investigated in this study was poor – even allowing for the limitations of the retrospective study design: almost one third (31.1%) of the discharge letters examined made no allowance for risk stratification and in less than one fifth (17.8%) of tumour episodes were recommendations for adjuvant treatment compliant with the guidelines. This is a serious issue, particularly in view of the researchers’ ‘sympathetic’ approach to the epicrises: through the methodology, all information available from all cases of a tumour episode was ultimately summarised as a virtual epicrisis, the cumulative information content of which was naturally greater than that of individual discharge letters. The clear discrepancy between the presence of (any kind of) treatment recommendation (93.7%) and its guideline conformity (17.8%) and – despite an increase in the information content of discharge letters – a decreasing guideline conformity of treatment recommendations between 2012 and 2014, suggest a poor and further declining knowledge of the guidelines. The lack of gender-specific differences with respect to information content and guideline conformity can, at the most, be seen as a gratifying incidental finding.

Of the risk-determining factors, the focality and the tumour size were documented only in 76.0% and 23.8% of the tumour episodes. Furthermore, the information content and guideline conformity of treatment recommendations following recurrent tumours deteriorated significantly compared to those following an initial NMIBC diagnosis. These observations confirm a suspicion expressed by our study group in a previous investigation that the risk profile for a recurrent and multifocal and larger than 3 cm tumour was not necessarily classed as high-risk and that such tumours were not given adequate attention [14]. At least the risk increase with respect to infiltration depth (pTa vs. pT1, CIS resp. pTa-1 with concomitant CIS) is associated with a significant increase in guideline compliant treatment recommendations.

The inclusion of the more than 12-year-old WHO-grading 2004 in less than two-thirds (62.2%) of tumour episodes also appears remarkable since a high-grade tumour is automatically classed high-risk irrespective of further risk-determining factors [7, 20, 22]. The issue of possible overtreatment regarding NMIBC appears to be of secondary importance, at least per our data. In addition to 42.6% not reliably effective treatment recommendations, a further 33.1% of recommendations – 68.8% (128/186) for intermediate and 26.7% (39/146) for high-risk – would result in an undertreatment (Table 1). This alarmingly high proportion counteracts the main objectives of the adjuvant treatment of NMIBC: the prevention, or at least delay of tumour recurrence or progression. This study focused on the quality of the discharge letters for NMIBC-patients with respect to risk stratification and guideline conformity.
Table 1. Treatment recommendations and guideline conformity according to risk profile

| Risk profile according to the information in the discharge letter | Data insufficient | Low | Intermediate | High |
|---|---|---|---|---|
| Clinic 1 | Clinic 2 | Clinic 3 | Clinic 1 | Clinic 2 | Clinic 3 | Clinic 1 | Clinic 2 | Clinic 3 | Clinic 1 | Clinic 2 | Clinic 3 |
| n | % | n | % | n | % | n | % | n | % | n | % |

**A**

- None: 1 (2.3) 2 (0.0) 0 (0.0) 0 (0.0) 6 (7.5) 0 (0.0) 6 (9.1) 2 (5.9) 1 (1.8) 6 (10.7)
- Second resection: 10 (22.7) 2 (4.7) 4 (10.7) 0 (0.0) 2 (15.4) 8 (10.0) 11 (27.5) 10 (25.2) 9 (26.5) 19 (33.9) 10 (17.9)
- Follow-up: 29 (65.9) 39 (90.7) 48 (68.6) 2 (100.0) 1 (100.0) 11 (84.6) 57 (71.3) 27 (76.7) 44 (66.7) 9 (26.5) 16 (28.6) 14 (25.0)
- Intraves. chemotherapy: 4 (9.1) 0 (0.0) 1 (14.3) 0 (0.0) 0 (0.0) 0 (0.0) 9 (11.3) 1 (2.5) 4 (11.8) 0 (0.0) 3 (5.4) 5 (8.9)
- Intraves. immunotherapy: 0 (0.0) 2 (4.7) 3 (4.3) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 1 (2.5) 1 (1.5) 14 (11.2) 13 (23.2) 16 (28.6)
- Radical cystectomy: 0 (0.0) 0 (0.0) 1 (14.3) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 4 (7.1) 5 (8.9)
- Radiation: 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0)

**B**

| Treatment recommendation | Data insufficient | Low | Intermediate | High |
|---|---|---|---|---|
| Clinic 2012 | Clinic 2013 | Clinic 2014 | Clinic 2012 | Clinic 2013 | Clinic 2014 | Clinic 2012 | Clinic 2013 | Clinic 2014 | Clinic 2012 | Clinic 2013 | Clinic 2014 |
| n | % | n | % | n | % | n | % | n | % | n | % |

- None: 7 (10.1) 2 (3.9) 2 (5.4) 0 (0.0) 0 (0.0) 0 (0.0) 6 (9.8) 3 (4.4) 3 (5.3) 5 (9.8) 3 (6.4) 1 (2.1)
- Second resection: 7 (10.1) 7 (13.7) 5 (13.5) 1 (25.0) 1 (14.3) 0 (0.0) 7 (11.5) 10 (14.7) 12 (21.1) 10 (19.6) 9 (19.1) 19 (39.6)
- Follow-up: 51 (73.9) 37 (2.7) 5 (7.5) 3 (75.0) 6 (85.7) 5 (100.0) 39 (63.9) 49 (72.1) 40 (70.2) 13 (25.5) 11 (23.4) 15 (31.3)
- Intraves. chemotherapy: 1 (1.4) 3 (5.9) 1 (27.3) 0 (0.0) 0 (0.0) 0 (0.0) 9 (14.8) 4 (5.9) 1 (1.8) 2 (3.9) 2 (4.3) 4 (8.3)
- Intraves. immunotherapy: 2 (2.9) 2 (3.9) 1 (27.3) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 1 (1.8) 1 (1.8) 15 (29.4) 20 (42.6) 8 (16.7)
- Radical cystectomy: 1 (1.4) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 6 (11.8) 2 (4.3) 1 (2.1)
- Radiation: 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 1 (1.8) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0)

A – according to clinic; B – according to years. Orange – not reliably effective recommendation; Green – guideline-compliant recommendation; Blue – undertreatment; Pink – overtreatment.
The study cannot provide answers to the question of whether and which adjuvant treatment patients actually received. For approximately one-third (31.1%) of the tumour episodes considered in this study, however, ambulatory urologists were unable to verify the guideline conformity of the almost standard (93.7%) treatment recommendations due to the lack of documentation of individual risk factors in the relevant discharge letters. This fact impedes both an effective and simple means of desired quality control, as well as the ambulant urologist in opting for an individually justified deviation from the guidelines. The study data provided no information on how fully and reliably all risk-determining factors were entered in surgery reports and ward notes. It can be assumed that clinic data is readily available [18]. If we follow this assumption, the information deficit presented in our investigation arises, above all, in the constitution of the discharge letter, which must therefore be branded as a ‘Bermuda Triangle’ of information transfer. This assessment provides a possible explanation for the observation by Chamie et al. that poor adherence to guidelines is largely physician-related, rather than patient- or tumour-related [13]. Continuous communication of the respective risk profile is therefore required; or, even better if clinics would inform ambulatory urologists of all known risk-determining factors. The authors recently presented a simple and cost-effective aid for the purpose [19]. Reliable risk stratification must be followed by a guideline compliant recommendation for adjuvant treatment of NMIBC. This requires better knowledge of guidelines – the study showed this to be particularly relevant in urological clinics – e.g. through relevant further training, consistent implementation of standard operating procedures (SOPs) and the participation of clinical and practicing urology professionals in tumour conferences. The lack of significant regional differences in respect of the information content of epicrises and the guideline conformity of treatment recommendations in a random cohort of 905 NMIBC cases from three German clinics over a period of three years is not evidence that the results given in this report reflect pars pro toto the quality of all epicrises for NMIBC-patients in Germany – although this possibility cannot be excluded.

CONCLUSIONS

Prospective data collation would help to verify or negate the study findings presented in this paper. These results have prompted the participating clinics to reassess the quality of discharge letters for NMIBC-patients. This article could also serve to motivate other colleagues to examine the quality of their discharge letters for NMIBC-patients with respect to adherence to the here examined quality criteria.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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