

Hospital costs of muscle-invasive urothelial carcinoma patients undergoing radical surgery: A French real-world retrospective study based on the national hospitalization database (PMSI)

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Introduction

- Urothelial carcinoma (UC) begins in the bladder or in the upper tract. Nearly 90% of UC are of bladder origin; the additional 10% are originating from the upper tract^{1,2}. In France, bladder cancer represented 13,074 cases and 5,355 deaths in 2018¹.
- In France, radical surgery (RS), defined as radical cystectomy for muscle invasive bladder cancer (MIBC) and nephroureterectomy for upper tract urothelial cancer (UTUC) is the standard of care for muscle-invasive urothelial carcinoma (MIUC) in localized stages. Neoadjuvant and adjuvant chemotherapies can be considered as potential additive treatment according to the localization of the disease²⁻⁵.
- After RS, patients remain at risk of recurrence over the course of disease. Prognosis of patients at high risk of recurrence is poor, with real-world median overall and disease-free survival of around 28 and 16 months respectively in France⁶. The recurrence could occur either locally (local recurrence [LR]) or at distance (distant recurrence [DR]). Management of patients with LR or DR is different, and the economic burden may be also different²⁻⁵.
- No economic data on MIUC patients who have undergone RS in France was retrieved from a literature search.
- The objective of this study was to describe incident MIUC patients who have undergone RS in France and the associated in-hospital costs over the course of the disease.

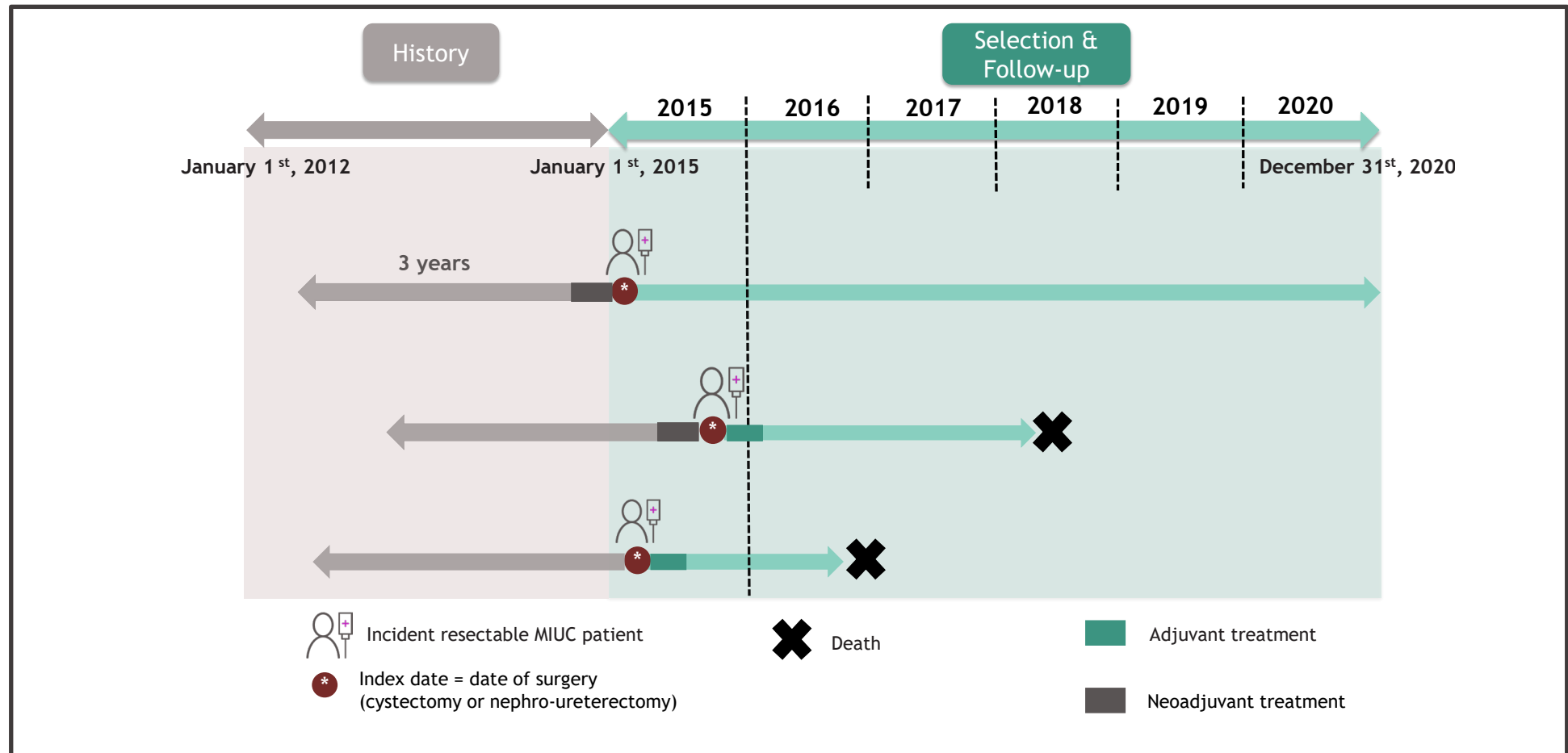
Methods

Study design

- This was a non-interventional national retrospective cohort study using secondary data from the French National Hospitalization Database (PMSI). PMSI database exhaustively includes hospital-related claims irrespective to healthcare insurance system or hospital settings (public/private). It is composed of four main domains: medicine, surgery and obstetric (MCO); home care (HAD); post-acute care and rehabilitation (SSR) and psychiatry⁷. Data from MCO, HAS and SSR were used to carry out this study.
- Study population included all adult resectable MIUC patients who underwent a first RS (index stay), between January 1st, 2015 and December 31st, 2015. Patients were described at index stay and were followed up to December 31st, 2020 or in-hospital death (whichever occurred first), to describe hospital costs over the course of the disease.
- Patients were defined as receiving neoadjuvant (NAC) or adjuvant (AC) chemotherapy if they received chemotherapy in the 6 months before or the 3 months after the index stay, respectively.

- Study design is presented in Figure 1.

Figure 1. Study design



Codes and inclusion/exclusion criteria

- Patients were considered as MIUC patients if they had a MIUC diagnosis, based on ICD-10 codes C65, C66 or C77 during index stay.
- RS was identified through French procedure classification (CCAM). Patients were considered as undergoing their first surgery if no surgery was identified within the 3 years prior to index stay. CCAM code was considered first for cancer location when it differed from ICD-10 code.
- Patients were excluded if they had a diagnosis of neuromuscular dysfunction of the bladder at index stay (ICD-10 N31) or markers of metastases (ICD-10 code or treatments) within 3 years prior to index stay, at index stay and/or within 3 months after index stay.

Costs considered and assessment of costs

- Costs included all the collected costs in the PMSI, presented in Table 1.

- Costs were measured only in patients with either MIBC or UTUC (i.e., those with both MIBC and UTUC at index stay were excluded from the analysis).

Table 1. Type of costs collected in the PMSI

Item	Definition
Stay	Stays in medicine, surgery, obstetrics, home care and post-acute care and rehabilitation
Expensive therapy (« liste en sus »)	Treatments administered during hospitalization and not included in DRG-related cost (e.g., pembrolizumab, avelumab, ...)
Intensive care unit admission	Admission to reanimation unit, intensive care unit
Emergency room admission	Admission followed or not followed by a in-hospital stay
Hospital specialist visits	Visits identified in public hospitals only

DRG: diagnosis related group.

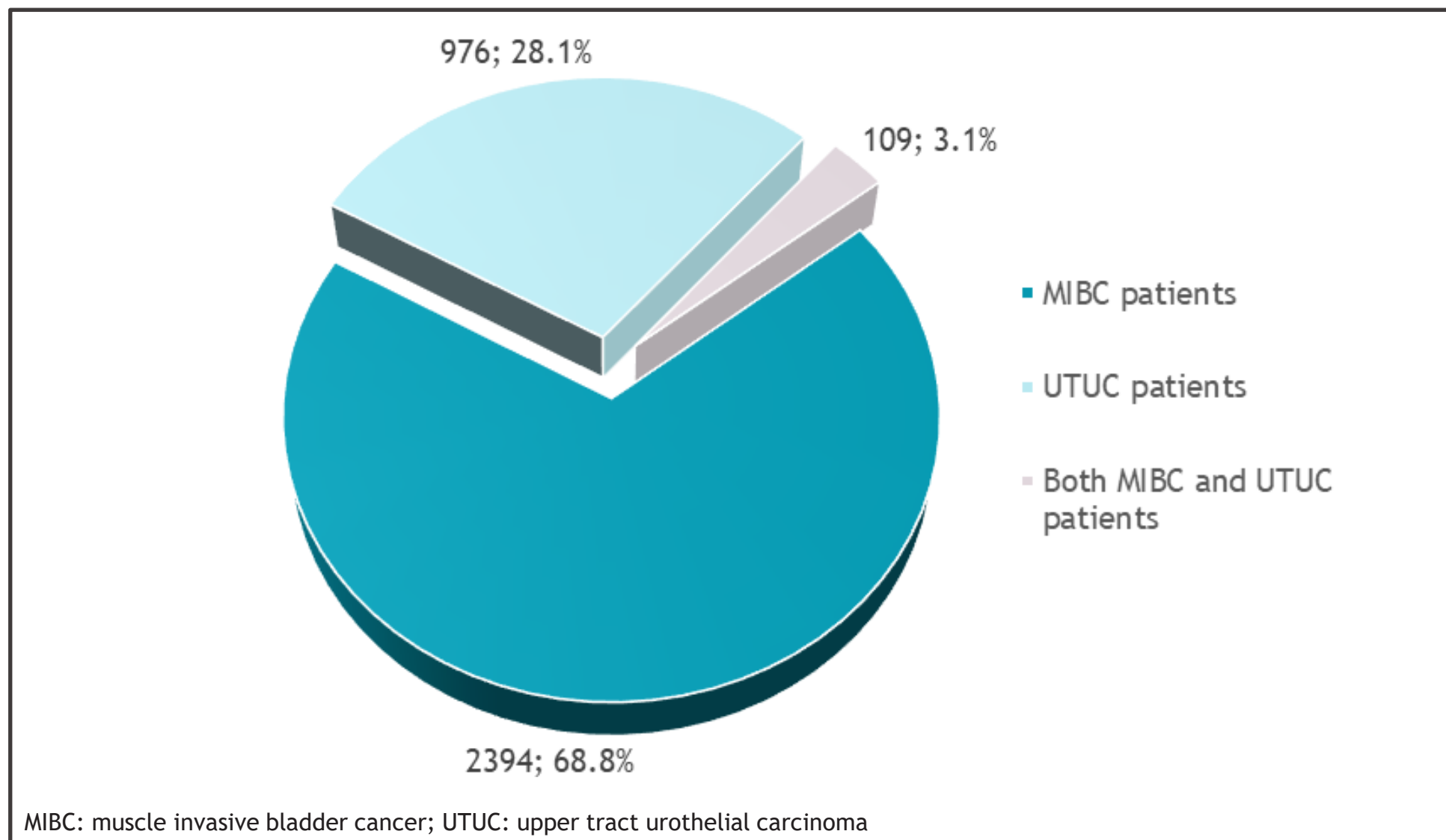
- Costs were described at index stay, and during follow-up at each stage of the disease (total after index stay, disease free, LR, DR).
- Costs were calculated as total and per-patient-per-month from a payer perspective and adjusted to €2020.
- Median follow-up and 95% confidence intervals were calculated thanks to the reverse Kaplan-Meier method⁸.

Results - Population description

Study population

- Figure 2 shows the 3,479 patients included. Among them there were:
 - 68.8% (N= 2,394) patients with MIBC,
 - 28.1% (N=976) patients with UTUC,
 - 3.1% (N=109) patients with both MIBC and UTUC.

Figure 2. Cancer location (N=3,479)



Clinical description of patients

- In 2015, the mean (±standard deviation [SD]) age of MIUC patients undergoing a first RS was 71.9 (±9.8) years old and was similar between MIBC and UTUC patients. Despite a high median age, 22.5% of patients were aged <65 years at the time of surgery with a minimum of 25 years (Table 2).
- The proportion of men was higher among MIBC patients (90.1%), than among UTUC patients (70.2%) (Table 2).
- The main comorbidities were relatively similar regardless of the cancer location, with diabetes, obesity, kidney disease, chronic pulmonary disease and peripheral vascular disease, recorded in more than 10% of the patients (Table 2).

Table 2. Characteristics of MIUC patients, by cancer location

	MIBC (N=2,394)	UTUC (N=976)	MIUC (N=3,370)
Male (n, %)	2,157 (90.1%)	685 (70.2%)	2,842 (84.3%)
Age			
mean (SD)	72.1 (9.5)	71.6 (10.5)	71.9 (9.8)
<65 years old (n, %)	527 (22.0%)	230 (23.6%)	757 (22.5%)
≥65 years old (n, %)	1,867 (78.0%)	746 (76.4%)	2,613 (77.5%)
Comorbidities with total frequencies >5% (n, %)			
Diabetes	524 (21.9%)	173 (17.7%)	697 (20.7%)
Obesity	397 (16.6%)	136 (13.9%)	533 (15.8%)
Kidney disease	381 (15.9%)	153 (15.7%)	534 (15.8%)
Chronic pulmonary disease	349 (14.6%)	86 (8.8%)	435 (12.9%)
Peripheral vascular disease	287 (12.0%)	87 (8.9%)	374 (11.1%)
Myocardial infection	239 (10.0%)	70 (7.2%)	309 (9.2%)
Congestive heart failure	158 (6.6%)	42 (4.3%)	200 (5.9%)
Cerebrovascular disease	144 (6.0%)	50 (5.1%)	194 (5.8%)

MIBC: muscle invasive bladder cancer; MIUC: muscle invasive urothelial carcinoma; SD: standard deviation; UTUC: upper tract urothelial carcinoma.

- Perioperative management of patients is described in Table 3. Most of the patients were treated with surgery only and did not receive NAC nor AC. Use of NAC or AC was more frequent in MIBC patients compared to UTUC patients.

Table 3. Perioperative management of MIUC patients, by cancer location

Perioperative management of patients	MIBC (N=2,394)	UTUC (N=976)	MIUC (N=3,370)
Radical surgery alone (n, %)	1,932 (80.7%)	928 (95.1%)	2,860 (84.9%)
Neoadjuvant chemotherapy + radical surgery (n, %)	330 (13.8%)	10 (1.0%)	340 (10.1%)
Radical surgery + adjuvant chemotherapy (n, %)	119 (5.0%)	36 (3.7%)	155 (4.6%)
Neoadjuvant chemotherapy + radical surgery + adjuvant chemotherapy (n, %)	13 (0.5%)	2 (0.2%)	15 (0.4%)

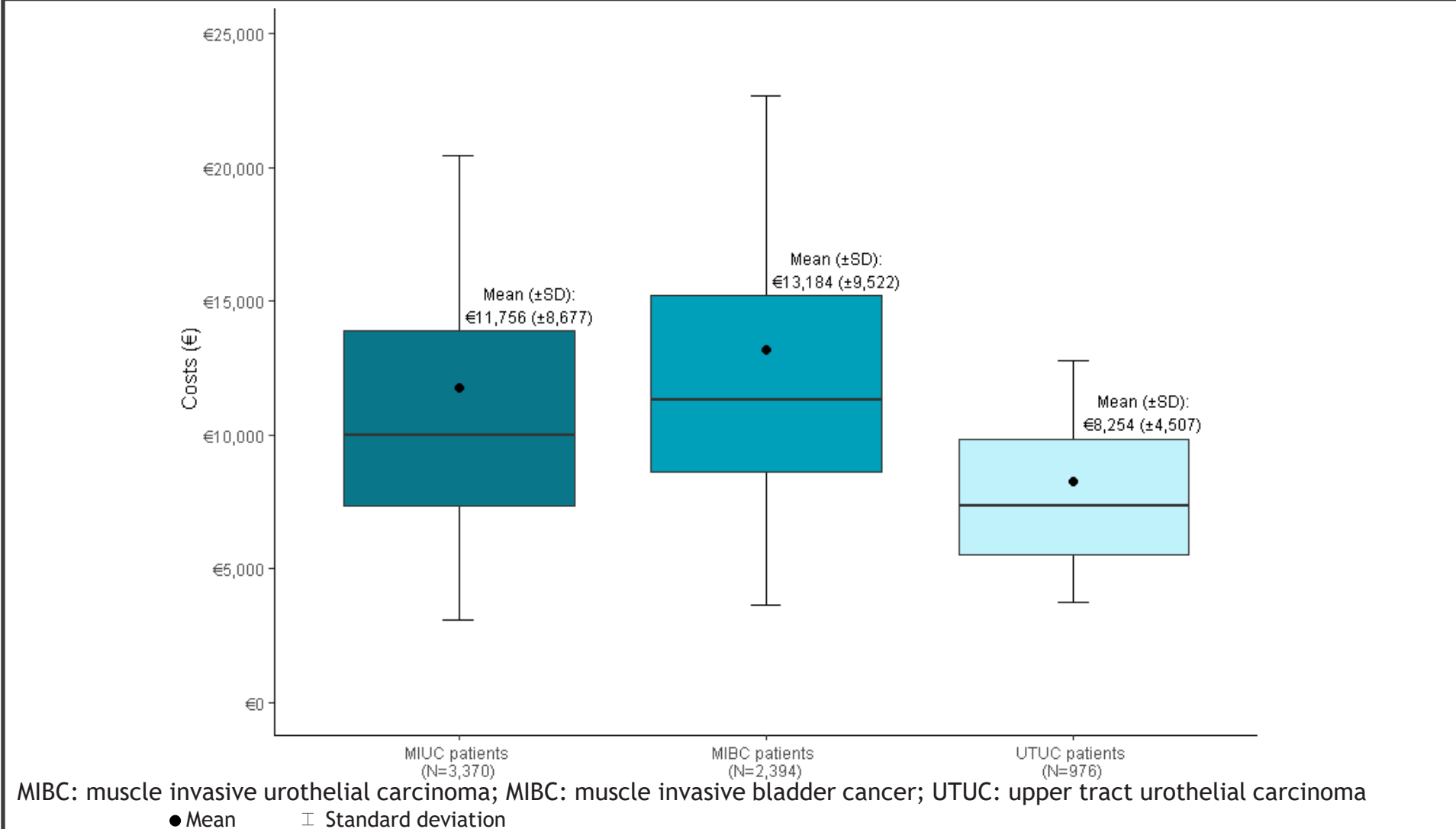
MIBC: muscle invasive bladder cancer; MIUC: muscle invasive urothelial carcinoma; UTUC: upper tract urothelial carcinoma.

Results - In-hospital costs

At initial RS

- In 2015, the mean (±SD) overall costs of first RS stay was €11,756 (±8,677) for MIUC patients. Overall costs were slightly higher for MIBC patients (€13,184 (±9,522)) than for UTUC patients (€8,254 (±4,507)) (Figure 3).

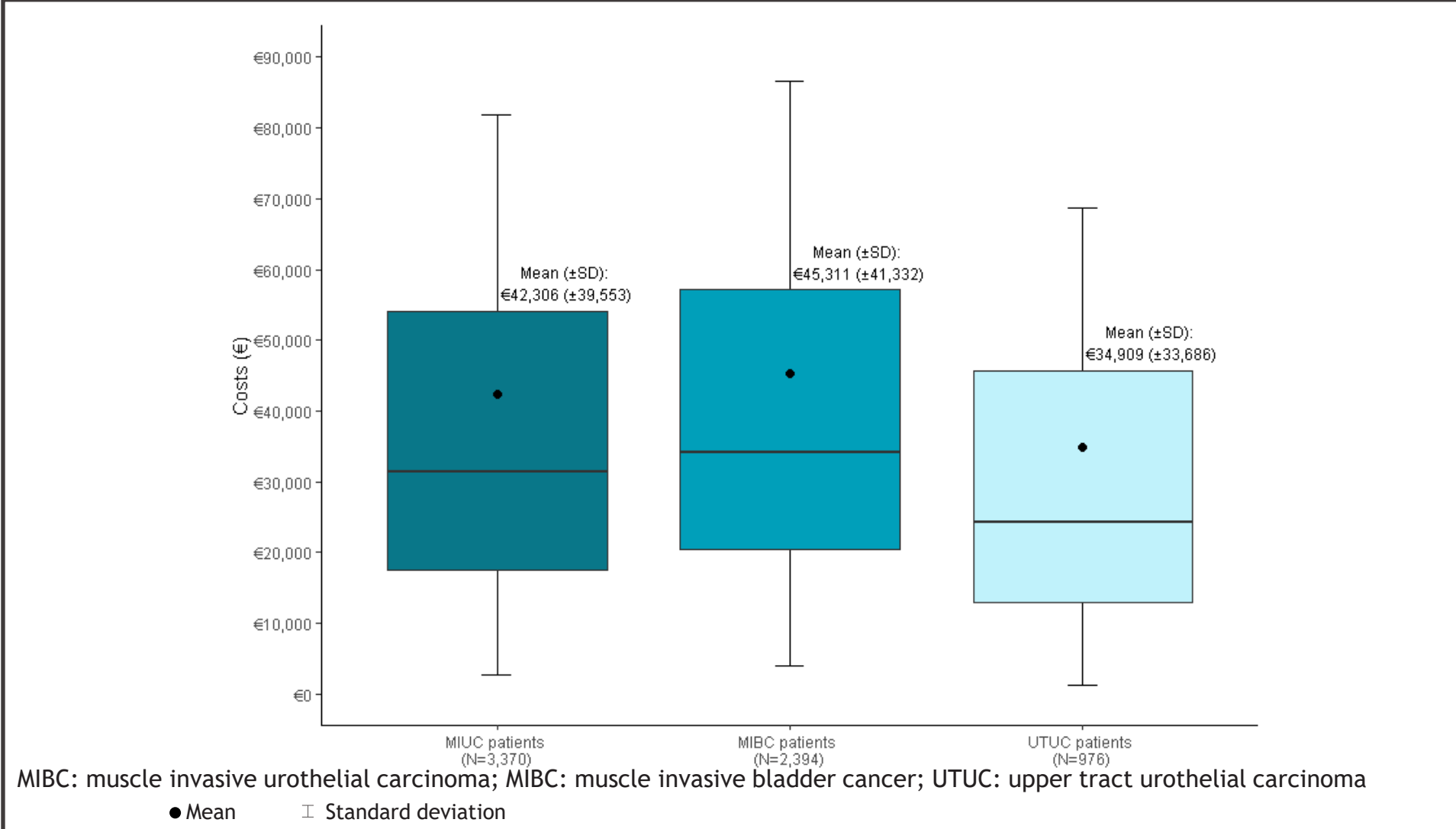
Figure 3. Overall costs for first radical surgery



Over whole follow-up period

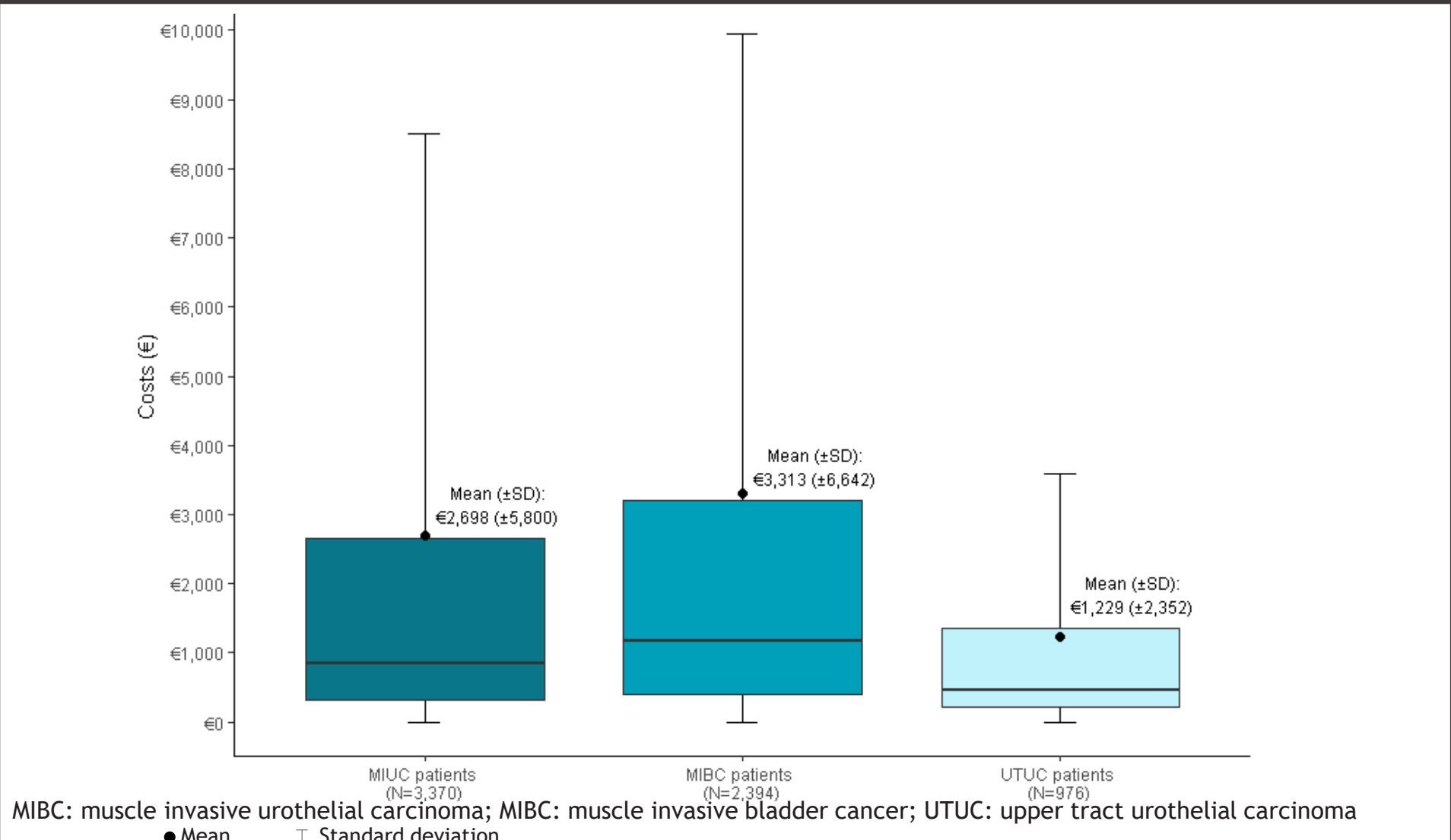
- For MIUC patients, median follow-up time was 66.0 months. Among these patients, 643 presented a LR (19.1%) and 1,612 a DR (47.8%).
- Over whole follow-up period, mean (±SD) overall costs (index stay excluded) were €42,306 (±39,553), €45,311 (±41,332) and €34,909 (±33,686) for MIUC, MIBC, and UTUC patient, respectively (Figure 4).

Figure 4. Overall costs over whole follow-up period



- Over whole follow-up period, mean (±SD) monthly overall costs (index stay excluded) were €2,698€ (±5,800), €3,313 (±6,642), and €1,229 (±2,352) for MIUC, MIBC, and UTUC patient, respectively (Figure 5).

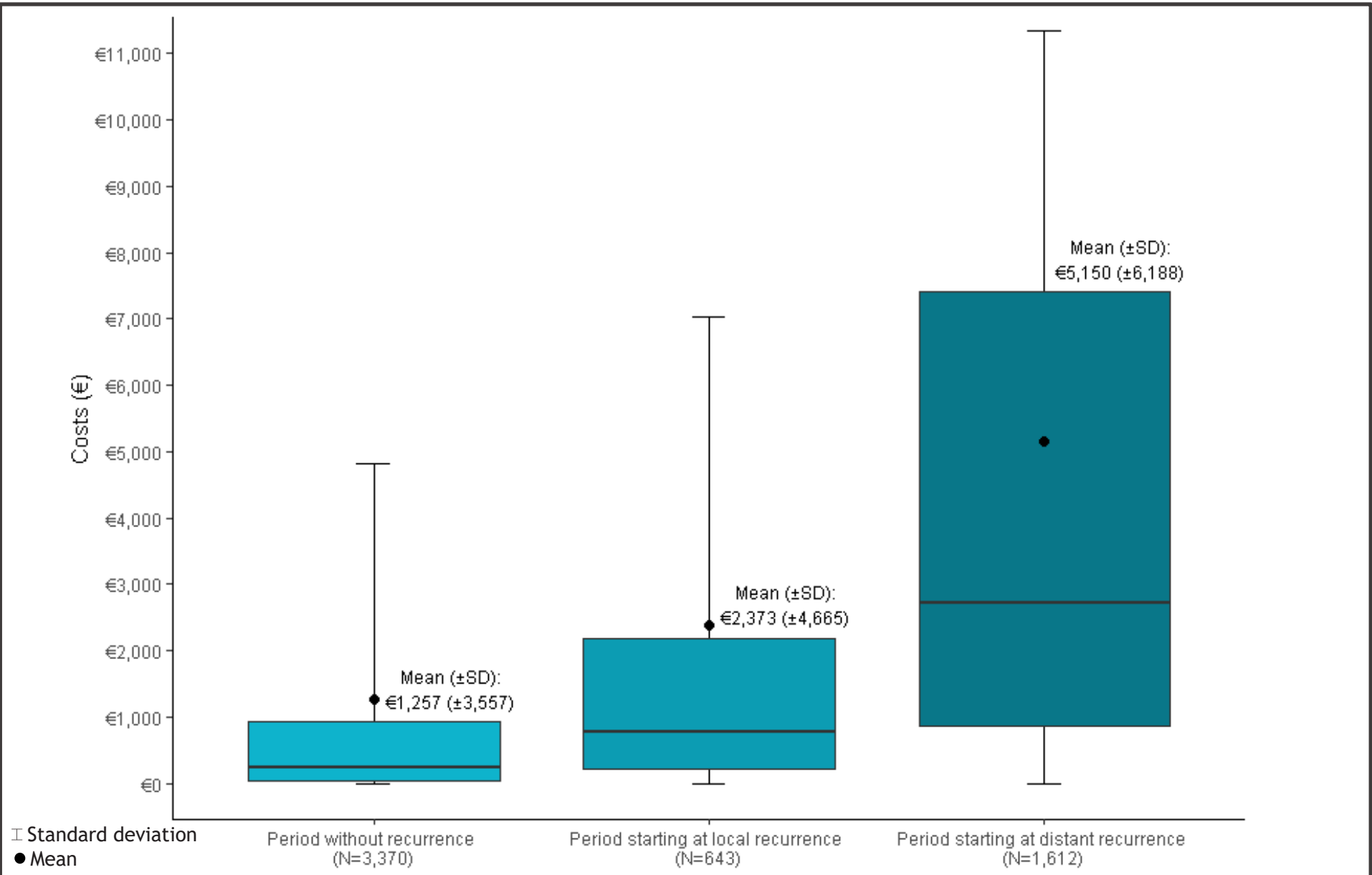
Figure 5. Monthly overall costs over whole follow-up period



In MIUC patients: breakdown by cancer location and health status

- As presented in Figure 6, Figure 7, and Figure 8, costs were increasing as the disease was progressing.
- For MIUC patients, mean monthly costs (±SD) without recurrence, with LR or with DR were €1,257 (±3,557), €2,373 (±4,665) and €5,150 (±6,188); respectively (Figure 6).

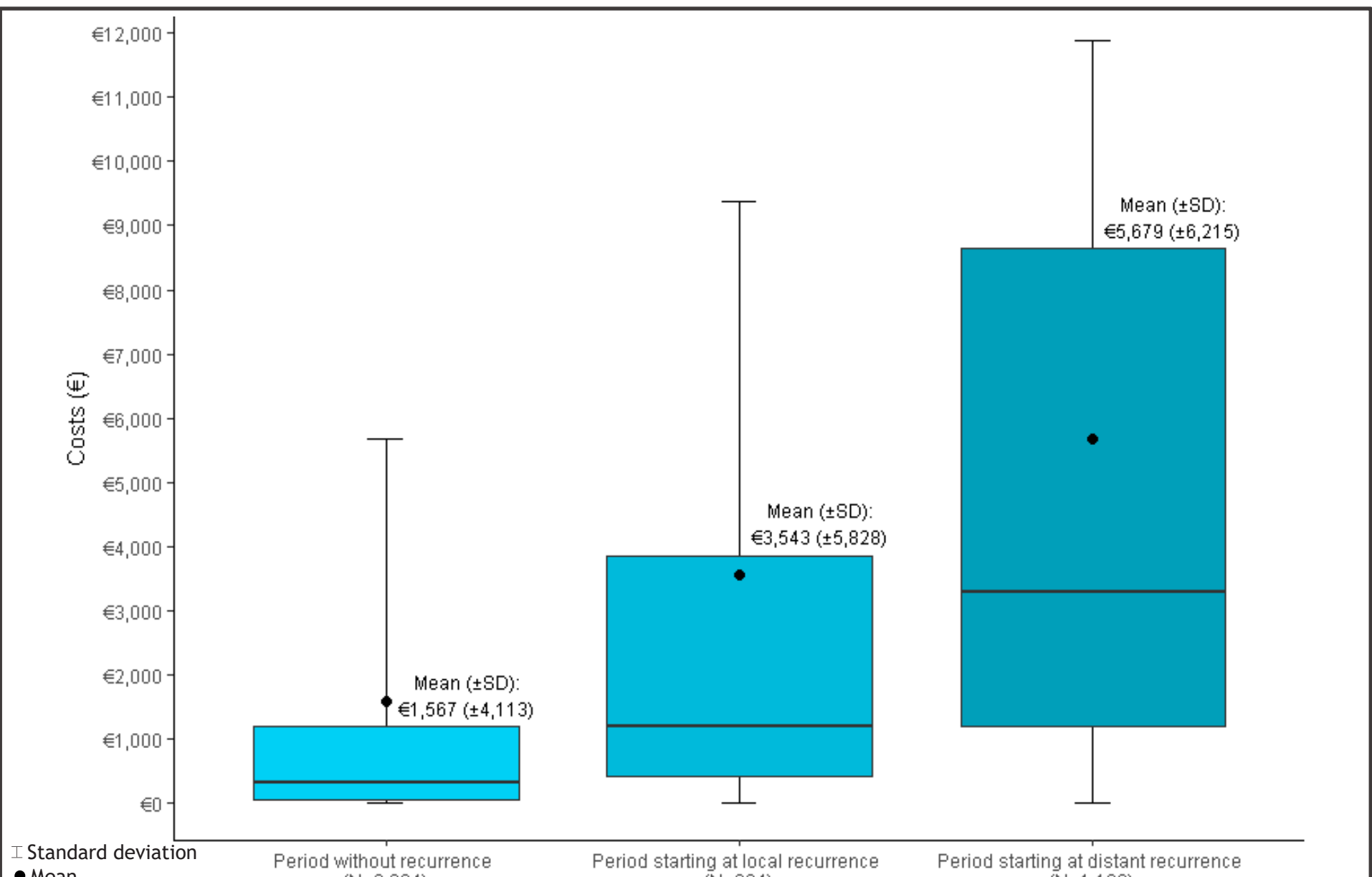
Figure 6. Monthly overall costs by health status-MIUC patients



In MIBC patients: breakdown by health status

- For MIBC, mean monthly costs (±SD) without recurrence, with LR or with DR were €1,567 (±4,113), €3,543 (±5,828) and €5,679 (±6,215); respectively (Figure 7).

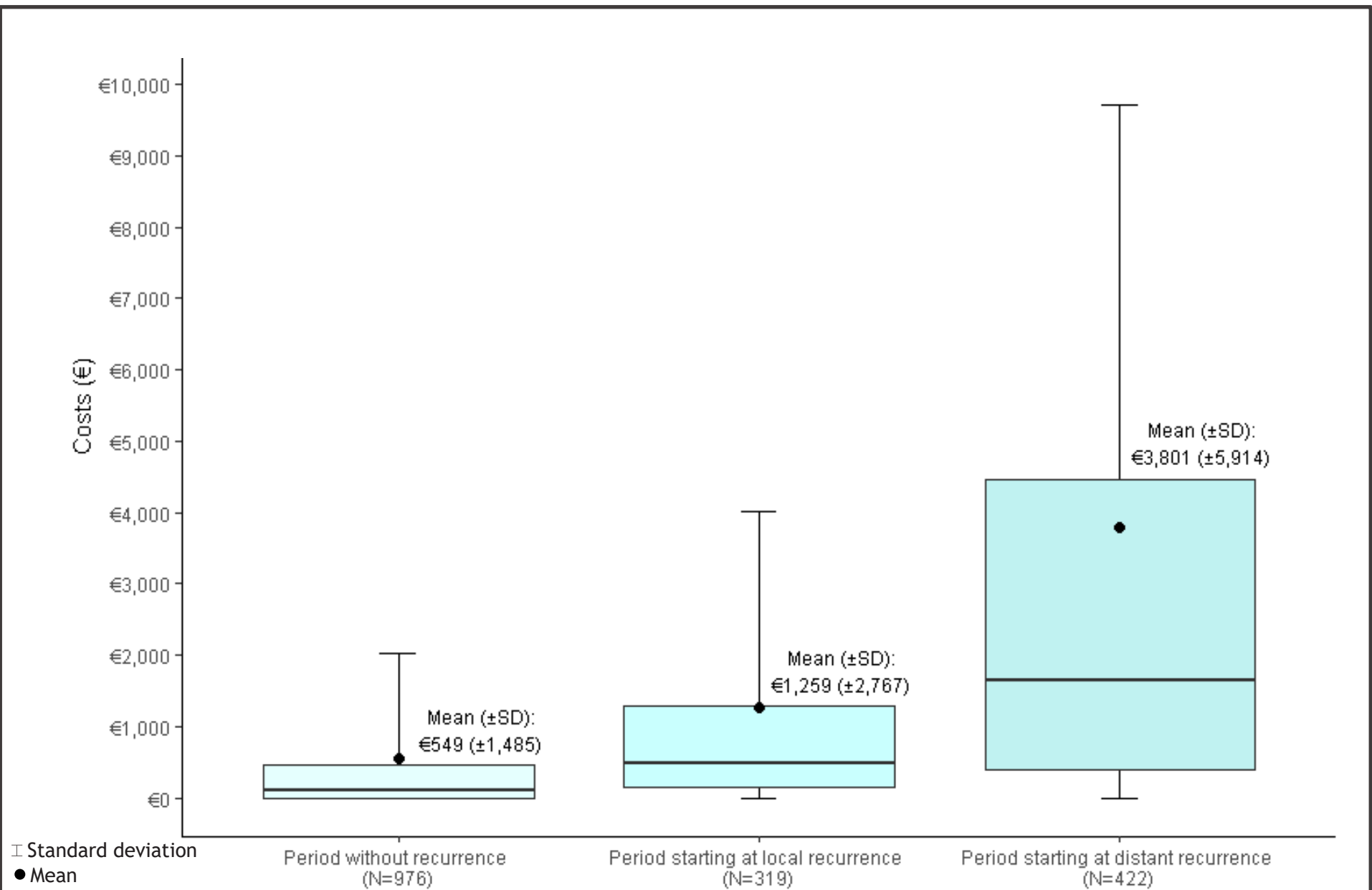
Figure 7. Monthly overall costs by health status-MIBC patients



In UTUC patients: breakdown by health status

- For UTUC, mean monthly costs (±SD) without recurrence, with LR or with DR were €549 (±1,485), €1,259 (±2,767) and €3,801 (±5,914); respectively (Figure 8).

Figure 8. Monthly overall costs by health status - UTUC patients



Conclusions

- This study provides the first and exhaustive real-world evidence of in-hospital costs related to MIUC patients who have undergone RS in France since 2015, with a maximum follow-up of 6 years.
- Patients' characteristics were consistent with those from the literature (age, sex) as well as comorbidities essentially linked to tobacco use, a well-known MIUC risk-factor. However, due to the common under recording of the comorbidities in the PMSI, the frequency of the comorbidities are likely to be underestimated⁹.
- This study cannot depict the exact repartition of MIBC and UTUC patients, since the focus is made only on those who have undergone RS and does not consider those who have undergone organ preservation strategies.
- MIUC led to high costs over the life of the patients, both during index stay for the RS and over whole follow-up period.
- Total and monthly follow-up costs were higher for patients with MIBC than for patients with UTUC.
- For both MIBC and UTUC, monthly costs were increasing as the disease was recurring (costs during disease-free < costs during LR < costs during DR).
- Due to the recent approval of innovative therapies for metastatic UC in France, such as avelumab as maintenance therapy, cost of patients with DR is likely to be underestimated in this study.
- Optimal patient management at an early stage, with new therapeutic options preventing patients from recurring, may prevent them from progressing to costlier stages.

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