A Comparison of Upper Tract TCC Treated Conservatively with Boari Flap or Laser Fulguration

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Abstract

We compare two conservative treatments for upper tract urothelial cancer (UTUC), laser fulguration and Boari flap. We review the indications for these treatments and the short (32 months) and long term (144 months) outcomes.

Methods: Retrospective analysis of 20 Boari flap patients and prospectively 13 laser fulguration patients.

Results: There was an all-cause mortality of 10% for the Boari group and 23% for the laser group (log rank P 0.19) at 32 months. There was 40% mortality at 144 months for the Boari group.

Conclusion: Oncological control can be effectively obtained with these conservative treatments. There was no significant difference between the two groups in terms of patient or tumour characteristics. The long term follow up for the Boari group can, with circumspection, be extrapolated to the laser group.

Keywords: Laser Fulguration; Boari flap

Abbreviations: UTUC: Upper Tract Urothelial Cancer.

Introduction

We are investigating whether there is any difference in the population, the tumour characteristics or the outcomes of a small number of patients treated for upper urinary tract TCC treated by two different conservative modalities, laser fulguration, our current practise, and local surgical excision with the Boari flap, our former practise. This conservative treatment is increasingly popular with the correct selection of patients with principally low risk UTUC to give equivalent oncological control when compared with traditional radical treatment, the radical nephro-ureterectomy [1,2].

Epidemiology, Pathology, Prognosis and Treatment

Urothelial cancer is the fifth most common cancer [3]. Upper tract urothelial cancer UTUC accounts for only 5-10% of this pelvicalyceal tumours are twice as common as ureteric [3,4]. Importantly 60% are invasive at diagnosis compared to only 20% of bladder TCC [5,6]. In concordance with this more aggressive stage at presentation, only few tumours of low malignant potential are found in the upper tract [7,8]. UTUC have a peak incidence at 70-90 years and are three times as common in men [9,10]. The most important risk factor is tobacco exposure which increases the relative risk from 2.5 to 7 [11,12]. UTUC often present after a bladder cancer.
The most common symptom is haematuria approx 75% [13,14]. Flexible ureteroscopy can visualise and biopsy to determine grade in 90% cases [15] with a low false negative rate. Conclusive diagnosis is fundamental to the decision making process. Ureteroscopy is also more accurate than CT Urogram and this can influence treatment decisions [16]. Confocal laser endomicroscopy can enhance the diagnostic accuracy [17] and biopsies can be performed with increasing accuracy [18]. Undergrading can occur after biopsy, so intensive follow up is necessary [19]. Prognosis is poor with muscle invasion and tends to be worse than bladder cancer [20]. The five year survival is <50% for pT2/3 tumours and <10% for pT4 [21-23]. Prognosis depends on many factors

Preoperative Factors

Sex is no longer an independent factor. Increasing age is associated with a worse disease specific survival although elderly can be cured [25,26]. Smoking increases risk for recurrence and mortality after RNU and recurrences within bladder [27-29]. Ureteric and multifocal tumours have a worse prognosis than renal pelvic tumours [23,30-33]. ASA score significantly correlates with cancer specific survival after RNU [34].

Postoperative Factors

The primary prognostic factors are stage and grade [35-37]. Management for localized disease with sparing of the kidney can be ureteroscopic with holmium, neodymium and thulium lasers [38], percutaneous or via an open surgical approach including the Boari flap. Endoscopic ablation can be used for low risk cancer if laser is available [39] with a flexible ureteroscope and complete tumour resection can be achieved. Close stringent follow up is needed particularly if high grade tumours are ablated. However, there is still a risk of under staging and under grading. Segmental ureteric resection with lymphadenectomy. Distal ureterectomy can be used for low risk tumour if they cannot be removed endoscopically and for high risk tumours when renal preservation is required [40-43].

Further, there is a shorter hospital stay and less loss of renal function with conservative treatment. The role of conservative treatment for low risk tumours has been defined as <2cm, single lesion, stage <T2 and low grade. The EUA recommendations for renal sparing management is Offer this as primary treatment for low risk tumours and two functional kidneys If patient has a solitary kidney or poor renal function providing it does not compromise oncological outcome High risk cancers if distal and in imperative cases such as solitary kidney or impaired renal function.

Methods

33 patients were treated conservatively for UTUC. This is a retrospective analysis for the Boari cohort and prospective for the laser cohort. Both are within one hospital trust. One surgeon performed the twenty Boari flaps from 2004 to 2015. Two further surgeons performed the thirteen laser fulgurations from 2014 to present. Patient and histological details were obtained from hospital electronic data bases. Statistical analysis was done using graph pad and Kaplan Meier graphs generated with excel. Laser used was a holmium 200um fibre 8-15Hz 8W Ureteroscopic follow up for the laser group had a first follow up at a mean of 4 months, then 6 monthly.

Results

Patient characteristics (Figure 1, Tables 1-3 & Graphs 1,2).
Boari patients | Laser patients | Significance
---|---|---
N | 20 | 13 |
Male/female | 7 (35%) 13 (65%) | 10 (77%) 3 (23%) | Fishers P = 0.032
Presentation
Haematuria | 10 (50%) | 7 (54%) |
Surveillance | 5 (25%) | 3 (23%) |
Incidental | 5 (25%) | 3 (23%) |
Smokers | 13 (65%) | 8 (62%) |
ASA score
1 | 5 (25%) | 0 |
2 | 10 (50%) | 5 (39%) |
ASA 1 and 2 | 15 (75%) | 5 (39%) | P = 0.067
3 | 5 (25%) | 6 (46%) |
4 | 0 | 2 (15%) |
ASA 3 and 4 | 5 (25%) | 8 (61%) | P = 0.067
Age years | Mean 71 median 72 | Mean 78.5 median 82 | t test P = 0.076
Creatinine uM | Mean 80 | Mean 111 | t test P = 0.55
eGFR ml/min/1.73m2 | Mean 70 | Mean 58 | t test P = 0.29

Table 1: Box plot age years.

| Grade | Boari | Laser |
|---|---|---|
| Not known 2 (15%) | 2 (15%) | P = 0.67
| 1 low | 6 (30%) | 2 (15%) |
| 2 medium | 11 (55%) | 5 (39%) 2Hg 3Lg | P = 0.76
| 3 high | 3 (15%) | 4 (31%) | P = 0.21

| Stage | Boari | Laser |
|---|---|---|
| pTa | 16 (80%) | 11 (85%) | P = 0.62
| pT1 | 1 (5%) | 0 |
| pT2 | 3 (15%) | 1 (8%) | P = 1.0

| Site within ureter | Boari | Laser |
|---|---|---|
| Proximal | 0 | 6 (46%) | P = 0.002
| Mid | 0 | 1 (8%) | P = 0.39
| Distal | 20 (100%) | 6 (46%) | P = 0.002
| Tumour size (mean) cm | 1.5 | 2.2 |
| Multifocality | 0 | 1 |
| Solitary kidney | 0 | 1 |
| Bladder recurrence | 3 patients 3 episodes | 3 patients 5 episodes | P = 1.0
| Subsequent radical nephro-ureterectomy | 2 | 2 | P = 1.0

Table 2: Tumour characteristics.

| | Boari 144 months | Boari 32 months | Laser 32 months |
|---|---|---|---|
| Recurrence | 8 (40%) | 2 (10%) | 8 (62%) |
| Mean time to recurrence | 13 months | 6 months | 4 months |
| Progression | 7 (35%) | 1 | 2 (15%) |
| Mean time to progression | 7.5 months | 6 months | 14 months |
| All cause mortality | 8 (40%) | 2 (10%) | 3 (23%) log rank chi squared 1.69 P = 0.19 |
| Survived at 32 months | 17 | | 3 |
| Disease specific mortality | 2/8 (25% of ACM) | 1 (50% of ACM) | 1/3 (33% of ACM) |
| Survival at 32 months | 89% | 89% | 64% |

Table 3: Prognosis.
Discussion

We have a series of 33 patients in total. As there are no significant differences in outcomes or patient/tumour profile so we can accept the survival curve of long-term Boari flap patients as representative of laser patients, albeit with caution. There are indications that have evolved as technology improves specifically with endourology making diagnosis and treatment more efficacious. Our laser population has an equal distribution of proximal and distal tumours (six and six) which is contrary to the trend of proximal dominance. Only three were invasive in the Boari group and one in the laser group, this was probably due to some under staging preoperatively, but the vast majorities on both groups are non-muscle invasive (85% in both groups). The patients tend to be elderly, however, our Boari group was younger with a mean age of 71 compared to 78 in the laser group but this was not significantly different. It is a disease that predominates in men, although our Boari group had more women (65%) although sex is no longer recognized as an important independent risk factor.

In both groups, the majorities were or had been smokers (65% and 62%). Few PUNLMPs are found in the ureter and indeed these formed the minority in both groups with 30% in the Boari and 15% in the laser groups of the eight measured tumour sizes all were small (<3cm) and only one was multifocal with two small lesions. Most present as haematuria 50% and 54% with the rest being...
diagnosed though bladder screening approx 25% or incidental findings 25%. Regarding renal function, there were three patients with impaired renal function. There was no significant difference in either the mean creatinine or glomerular filtration rate between the two groups. One patient within the laser group had a solitary kidney. The ASA scores were summated into two groups, ASA 1 and 2 and ASA 3 and 4. There were more unfit patients in the laser group (61%) compared to the Boari group (25%) but this was not significant statistically.

We have treated four high grade patients within the laser group as have others with good outcomes. One of these resulted from upgrading from a G2 biopsy. One patient was upstaged to muscle invasive pT2 disease and underwent radical nephroureterectomy two months later, with survival of 13 months so far. Another patient had radical nephroureterectomy 10 months later and died 4 months after this operation, 15 months after the original laser procedure. A further patient has died at 26 months post-surgery. The other shows survival at 19 months. Within the Boari group there were three high grade and pT2 stage of which two did not have biopsies. The other was upstaged from pT1 to pT2. They have subsequently died at 15, 49 and 50 months. T3 t4 can be treated in carefully selected pts. Two patients G1pTa and G2pTa underwent subsequent nephroureterectomy dying at 6 and 109 months respectively, 6/13 laser patients had intravesical therapy with 4 having BCG and 2 having MMC. There was no significant difference in bladder recurrence. Looking at all 33 patients and the 11 deaths to summarize the effect of stage on mortality. 8/11 deaths were pTa disease, and 3/11 were pT2. As regards grade, less than half the mortalities were high grade G3, 5/11 patients. 3/11 patients were G2 and 3/11 patients were G1. The ASA score was also distributed evenly. 5/11 patients were ASA 3, 3/11 patients were ASA 2 and 3/11 patients were ASA 1. Both methods of treatment were equally efficacious with a long term survival of 65% at 9 years.

We followed up both groups for 32 months. There were two deaths from all cause in the Boari group and three in the laser. All had ureteric recurrences. Log rank analysis did not show any significant difference (P=0.19). One death in each group was due to disease progression. We have added the long term follow up the Boari group to illustrate long term survival of 65% at nine years.

Criticisms

The number of patients is small. It has a retrospective arm and there may be a selection bias in patients. No comparison with radical nephroureterectomy, however we do have a long follow up for Boari arm.

Conclusion

Good oncological control can be achieved with renal sparing treatments. The newer endoscopic is as efficacious as the Boari flap.

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