

Dear Doctor,

Greetings from Micro Labs limited. We are happy to bring you “**NU Rounds**” which contains latest and interesting news in the field of Urology.

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Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Ltd



Novel selective β_3 -adrenoreceptor agonist vibegron for treatment-resistant monosymptomatic nocturnal enuresis in children

While desmopressin and alarm therapy are the typical first-line therapies for monosymptomatic nocturnal enuresis (MNE), treatment resistance is seen in about 50 percent of patients, particularly in OAB children. Mirabegron, the first β_3 -AR, is widely used in the treatment of OAB in adult patients because β_3 -AR relaxes the smooth muscle of the detrusor and improves the flexibility of the bladder, while having a detrimental effect on the frequency of the bladder contraction needed for voiding. The medication can therefore be prohibited in children owing to its damage to reproductive cells. In Japan, vibegron, a new, potent and highly selective β_3 -AR with no reproductive side-effects, has recently been created.

A phase III randomized, double-blind, placebo-controlled study showed that vibegron is useful and safe for the treatment of adult OAB patients in Japan. Additionally, a post-hoc review utilizing the results from the Phase III research reported that vibegron greatly decreased the incidence of nocturnal voiding by growing the amount of the first morning voiding, contributing to extended hours of undisturbed sleep in OAB patients. The authors present here their first report on vibegron's efficacy for refractory MNE in children. Between February 2019 and December 2019, at the Saitama Children's Medical Center, 24 Japanese children with MNE refractory (median age 10.5 years; range 7.5–17.3; males $n = 17$), who were defined as non-responders to standard treatments, including desmopressin, were enrolled in the current retrospective study. They used the Dysfunctional Voiding Symptom Score, and in children with no lower urinary tract symptoms, MNE denoted enuresis according to the terminology of the International Children's Continence Society. Before the initiation of vibegron, all patients with enuresis were non-responsive to standard treatments, including desmopressin melt ($n = 24$; median duration of treatment 10.7 months), alarm therapy ($n = 19$; 14.7 months), solifenacin ($n = 23$; 7.5 months) and imipramine ($n = 8$; 3.2 months), with a median of 15.4 wet nights per 4 weeks (interquartile range 10.8–21.3).



A single daily dosage (25 mg) of vibegron, upon receiving informed consent (Beova; Kissei Pharmaceutical Co., Tokyo, Japan) was provided as a supplemental therapy for 4 weeks after the evening meal. During the 4-week treatment with vibegron, the median number of wet nights was significantly reduced from 15.4 to 6.8 days (56% reduction, $P < 0.001$), and the median maximum VV was significantly increased from 240 to 300 mL (25% increase, $P < 0.005$). CR (100% reduction) and PR (50–99% reduction) were achieved in three and nine patients, respectively (response group). There were no variations in clinical features, such as race, number of wet nights before vibegron, age at vibegron initiation, and form of concomitant therapies (i.e. desmopressin, alarm therapy, solifenacin, and imipramine) between response ($n=12$) and non-response ($n=12$) classes. However, in the response community, the frequency of constipation involving laxative usage was significantly higher than in the non-answer category (67% vs 8%, $P < 0.001$). Vibegron was well tolerated throughout the study period, and no harmful drug-related effects were found.

Authors claim this is the first research to show, to the best of their understanding, that vibegron can be a valuable therapeutic alternative for refractory MNE, particularly in constipated children. The authors found that vibegron substantially decreased the occurrence of wet nights by growing the capacity of the bladder at night without adversely impacting constipation in children with MNE. Non-responding children with enuresis typically have constipation, which can affect the functioning of the bladder and result in OAB symptoms. Anticholinergic agents remain the pillar of treatment approach as the first-line therapy for patients with OAB. Due to its low efficacy and high constipation associated with the drug, monotherapy with anticholinergic agents is not recommended for MNE children. The aforementioned Phase III randomized controlled study showed that the incidence of drug-related adverse events with vibegron was similar to that with placebo and less than with anticholinergic agents. In addition, a retrospective study has shown that constipation has a negative impact on the response to desmopressin, particularly in patients with Strict enuresis. The authors suggest vibegron as the first b3-AR that would be approved for the treatment of refractory MNE, especially in constipated children. The present study is, however, limited by the reported retrospective nature of a single centre. In comparison, the amount of patients to draw valid conclusions in the present analysis was quite limited. Further multicenter, prospective randomized controlled studies are therefore warranted for assessing vibegron efficacy and safety in children with refractory MNE.

Source: Fujinaga S, et al. Efficacy of the novel selective b3-adrenoreceptor agonist vibegron for treatment-resistant monosymptomatic nocturnal enuresis in children. Jap Urol Assoc. May 2020. DOI: 10.1111/iju.14264



Post robotic partial nephrectomy: Trocar site recurrence

INTRODUCTION

Throughout cancer surgery and tumor therapy, tumor cell spillage may occur direct seeding of the cancer cell in the surgical wound. Surgery concerning laparoscopic cancer is no exception. In fact, it has been well reported that recurrence of tumors develops at trocar sites in the surgical oncology literature, resulting in recurrence of trocar sites (TSR). TSR became a unusual occurrence after laparoscopic urological surgery with an incidence varying from 0.03% to 0.09% for renal cell carcinoma (RCC). Tumor biological aggressiveness and laparoscopic-related immune reaction are suspected to be the culprits alongside spillage of cancer cells. The real TSR etiology is not well known and little recognized in the deceased. RCC has, however, been shown to be one of the least of all abdominal malignancy complicated by TSR or peritoneal seeding. The role of robotic partial nephrectomy (RPN) in the treatment of RCC has been established with an oncological outcome comparable to that of open approach. The robotic surgical system Da Vinci[®] improves dexterity, increases visualization and filters the operating surgeon's tremor. It also improves ergonomic setting to boost personal comfort for surgeons. The use of robotic procedure in nephron-sparing surgery has grown and has culminated in expanded familiarity of RPN for managing low renal mass (SRM). The technique and both functional and oncologic outcome of RPN was replicated by multiple authors from different centers.

In this article the authors report to highlight their presentation on the incidence of TSR after RPN in relatively large series of patients. They reviewed the literature to identify specific factors related to TSR.

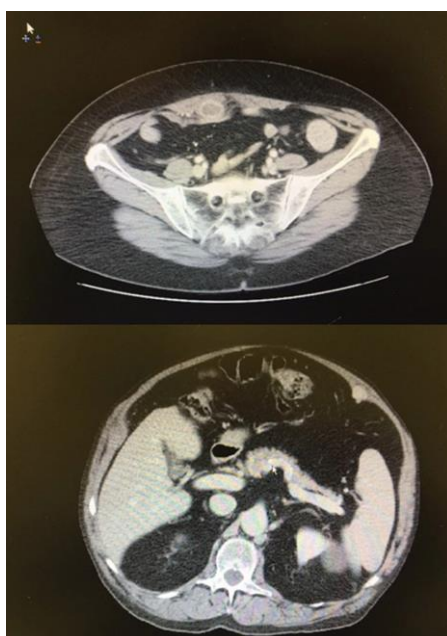
METHODS

The data about patient who underwent RPN was prospectively reviewed. Medical record of the patients were reviewed who had the diagnosis of RCC on the final pathology. The patient with TSR and demonstrated their presentation was identified and treatment along with the outcome.



RESULTS

A total of 335 patients underwent RPN during the study period for renal mass. Two hundred and sixty-nine (80.3%) patients were found to have RCC on the final pathologic evaluation of their mass. Two patients were identified (0.7% of all the RCC in the study) who developed TSR during an average follow-up period of 31 months (ranging from 18 to 72 months). The first recurrence appeared 18 months after the surgery. The second recurrence presented 72 months after RPN. Both cases underwent open surgical excision of the trocar site, in which the recurrence appeared.



Renal cell carcinoma recurrence at the trocar site. In the first case, the recurrence occurred in the trocar used for clamping, and in the second picture, the recurrence developed in the 8-mm trocar used for robotic instrument

CONCLUSIONS

RCC recurrence can pose as TSR after RPN, but it is uncommon and underreported. During surveillance follow-up of RCC treated with RPN, careful attention should be given to inspecting the trocar region. After surgery it can develop for up to 72 months. Growing time a lump forms after surgery, surgical removal of the trocar site should be treated with large excision. Further studies are needed to understand the etiology behind this type of recurrence, so that it can be avoided.

REFERENCE

Salkini MW. Trocar site recurrence after robotic partial nephrectomy to treat of renal cell carcinoma. Urol Ann 2020; 12:112-5.



In patients with muscle-invasive bladder cancer (MIBC) Frailty is significantly associated with the type of urinary diversion

INTRODUCTION

The normal surgical procedure for MIBC is urinary diversion after RC. Of the types of urinary distraction, orthotopic Neobladder (ONB) reconstruction is a continental urinary distraction procedure; however, it is not suitable for each patient due to the complexity of the procedure, increased levels of surgical stress and higher complication rates compared to other non-continental procedures, such as ileal conduit and cutaneous ureterostomy. Although a patient's selection for an ONB reconstruction is strict, the optimal tools for ONB patient selection are not available except for contraindications, such as pre-existing renal or liver impairment, or prostatic involvement for the bladder neck. The decision to select urinary diversion currently depends on factors relating to clinical experiences and surgeons. Interest in frailty has recently increased, with high numbers of elderly patients worldwide. Since frailty can be used as an indicator of biological function, it may be helpful to advise collection of therapies. However, the impact of frailty on the option of urinary diversions, such as ONB, ileal conduit, or cutaneous ureterostomy, has not yet been studied. There is still inadequate data on effective frailty evaluation instruments, as the frailty tests appear to measure various frailty features. The impact of frailty on urinary diversion selection in MIBC patients who were treated with RC was examined in this research (FRAUD study).

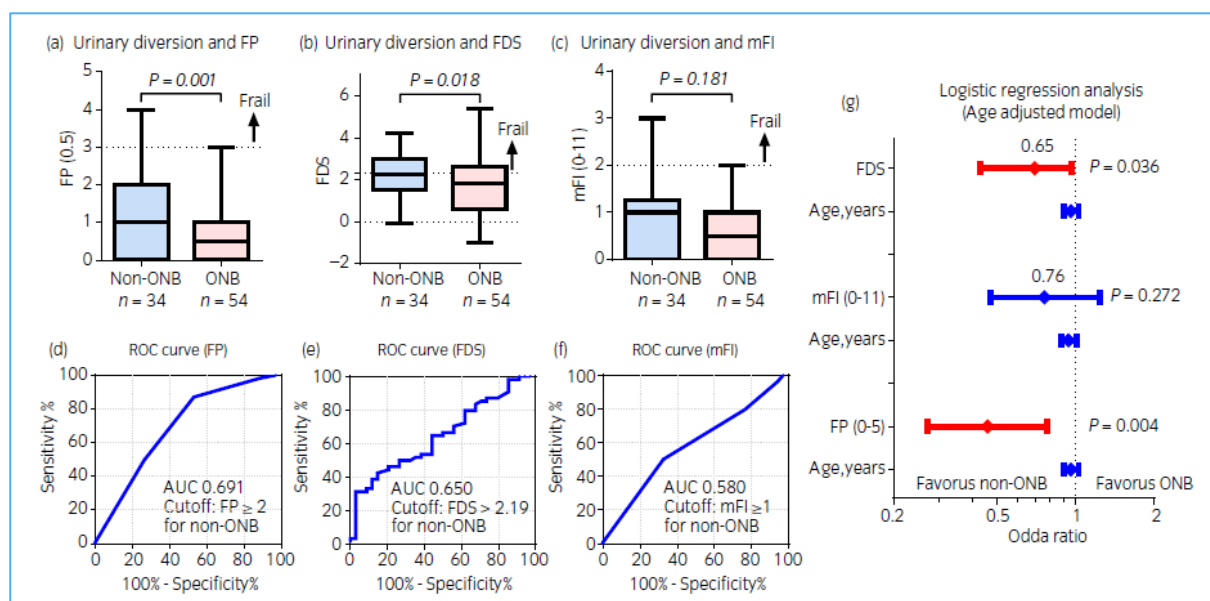
METHODS

Between January 2014 and January 2020, the authors prospectively evaluated frailty in 88 patients with localized muscle-invasive bladder cancer, who had received radical cystectomy and urinary diversion. The selection of the type of urinary diversion was determined by the operating surgeon based on performance status, comorbidities, tumor status and the patient's preference. The frailty evaluation included the Fried phenotype criteria, the modified frailty index and the frailty discriminant score. They investigated the association between frailty and type of urinary diversion, the effect of frailty on postoperative complications and the effect of frailty on overall survival.

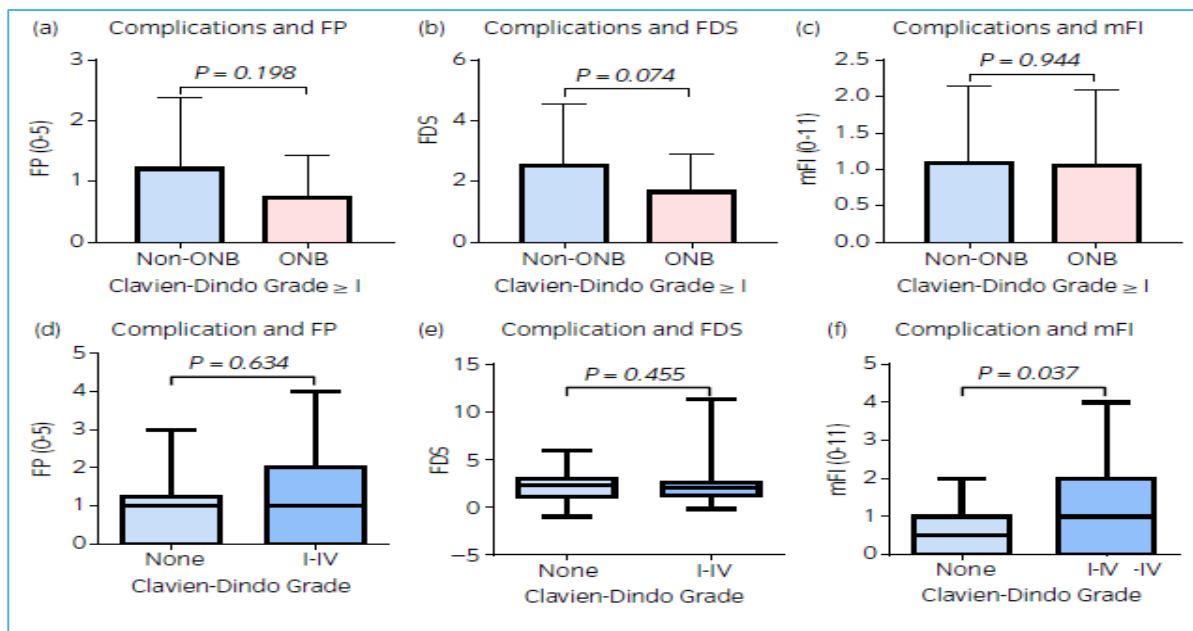


RESULTS

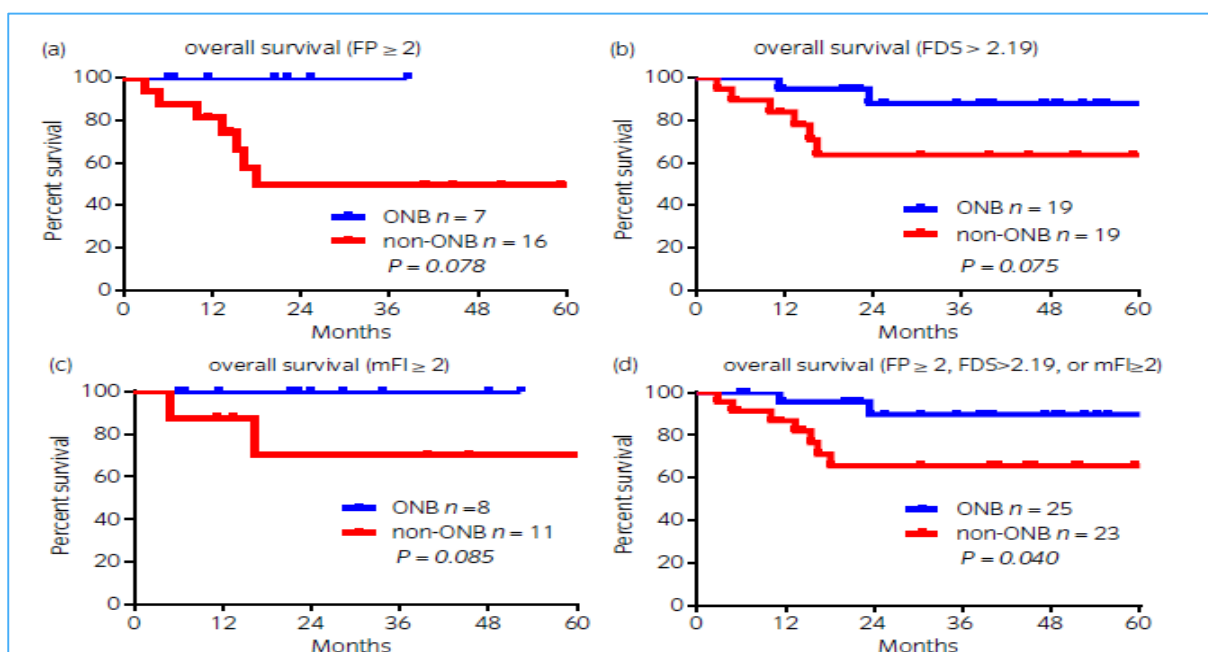
The median age of the selected participants was 68 years. The number of patients with an orthotopic neobladder and any postoperative complications was 54 (61%) and 46 (52%), respectively. Of the frailty assessment tools that were used, Fried phenotype criteria and frailty discriminant score were significantly associated with the selection of non-orthotopic neobladder urinary diversion. Occurrences of postoperative complications in participants were significantly associated with modified frailty index, but not with Fried phenotype criteria and frailty discriminant score. Multivariate Cox regression analysis showed that a higher frailty discriminant score was significantly associated with poor overall survival, whereas higher Fried phenotype criteria and modified frailty index were not.



The effect of frailty on urinary diversions. The frailty between the patients with ONB and non-ONB (ileal conduit or cutaneous ureterostomy) is compared using the (a) FP, (b) FDS and (c) mFI. The optimal cut-off value for non-ONB selection of (d) FP, (e) FDS and (f) mFI were evaluated using ROC curve analysis. (g) The effect of frailty on selection of urinary diversion was evaluated by age-adjusted logistic regression models



The effect of frailty on postoperative complications, prevalence of frailty and agreement of different frailty assessment tools. The association between the frailty and postoperative complications is compared using the (a) FP, (b) FDS and (c) mFI between the patients with non-ONB and ONB. The association between the frailty and postoperative complications is compared in (d) FP, (e) FDS and (f) mFI in all patients.



Overall survival in patients with frailty. Overall survival in patients with any frailty was compared between the patients with ONB and non-ONB by the (a) FP ≥ 2 , (b) FD > 2.19 and (c) mFI ≥ 2 . (d) Overall survival in patients with combined definition of frailty (any of FP ≥ 2 , FDS > 2.19 or mFI ≥ 2) was compared between the patients with ONB and non-ONB



CONCLUSION

Frailty is strongly linked to the type of urinary diversion, and in patients undergoing radical cystectomy frailty should be considered for the selection of urinary diversion in muscle-invasive bladder cancer.

REFERENCE

Okita K, et al. Frailty is significantly associated with the type of urinary diversion in patients with muscle-invasive bladder cancer. Int. J. Urol. May 2020. doi:[10.1111/iju.14263](https://doi.org/10.1111/iju.14263)



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