Urol Res (2004) 32: 298–303
DOI 10.1007/s00240-004-0417-7

ORIGINAL PAPER

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Bladder augmentation with an omental pedicled gastric seromuscular flap without the necessity of gastric resection

Received: 5 December 2003 / Accepted: 3 March 2004 / Published online: 21 April 2004

Abstract Bladder augmentation using gastrointestinal segments requires gastric or intestinal resection. This has several risks. In a rat model, we aimed to test the efficacy of a new procedure in which a gastric seromuscular (GSM) flap is separated from the gastric mucosa without the necessity of gastric resection, and this GSM flap, based on an omentum pedicle, is transferred to the bladder. A GSM flap based on an omental leaf was dissected from the gastric mucosa and rotated 180° counter-clockwise, after ligation of the vessels relating to the omentum, until the mid-duodenum. After urodynamic analysis for control levels of bladder capacity and pressure, the GSM flap was anastomosed to the bladder with a continuous suture. Because four rats died due to bladder calculi, only 21 of 25 rats were killed at 1 month ($n = 10$) and 4 months ($n = 11$) for histopathological and urodynamic evaluations of the augmented bladder. Bladder capacity increased significantly in the augmented bladders compared to preaugmentation ($P < 0.001$). There was no significant difference between end-filling pressures of the augmented bladders and preaugmentation. Histopathological findings demonstrated that the muscular surface of the flap was completely re-epithelialized in all rats. Squamous metaplasia was detected in 30% (3/10) of the 1 month group rats, and in 55% (6/11) of 4 month rats ($P > 0.05$). Gross calculi formation appeared in 20% (2/10) of the 1 month group rats, and in 34% (4/11) of 4 month rats ($P > 0.05$). Our data show that the use of the GSM flap in the bladder of a rat resulted in the complete re-epithelialization of the flap and sufficient bladder capacity. Despite significant complications such as death, metaplasia and calculi, this technique may be considered as an alternative experimental model to traditional full-thickness patching, which needs gastric or intestinal resection.

Keywords Bladder augmentation · Omentum · Gastric seromuscular flap

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Introduction

Various alternatives for augmentation cystoplasty have been widely used clinically for the last five decades [1]. Small and large bowel, stomach and megaureters are still the most commonly proposed. However, gastric or intestinal resection is required for seromuscular cystoplasty as well as other augmentation techniques using gastrointestinal segments [1, 2]. The risks of gastrointestinal resection include intraperitoneal contamination, anastomotic leakage, reduced stomach size, shortened intestine, intestinal dysmotility and an additional operative procedure [3, 4]. To prevent these complications, we describe a new procedure in which a gastric seromuscular (GSM) flap was obtained without the necessity of gastric resection, and a GSM flap with an omental pedicle was placed onto the bladder.

Materials and methods

This study was performed with the approval of the Animal Investigation Committee of Akdeniz University School of Medicine. A total of 25 young adult female Swiss albino rats, weighing between 150 and 270 g were kept in individual cages, fed standard rat chow and given water ad libitum. On the day before the operation the diet was changed from regular chow to a liquid diet. Surgical procedures were performed, after an overnight fast, using sterile techniques. All rats were anesthetized intramuscularly with xylazine (10 mg/kg) and ketamine (50 mg/kg). The study consisted of two phases; augmentation cystoplasty with omental pedicled

seromuscular flap, and killing the rats at 1 or 4 months postoperatively. The rats were divided into two groups according to the time of death: those killed at 1 month ($n=10$), and those at 4 months ($n=11$). Four rats died of complications prior to analysis, one from the 1 month group and three from the 4 month group.

Augmentation cystoplasty

The procedure was performed through a midline incision using a magnifying lens. The gastrocolic ligament was opened to expose the posterior surface of the stomach. In rats, the relationship between the omental and gastroepiploic vessels commonly ends at the middle of the greater gastric curvature, and the omental leaves extend to the duodenum and spleen. A semi-elliptical incision measuring approximately 10×15 mm was outlined horizontally from the region where the collateral circulation between omentum and gastroepiploic vessels disappeared to the pyloric antrum, and coronally from the posterior gastric surface to the anterior gastric surface (Fig. 1A). The GSM flap was gently separated from the gastric mucosa with blunt and sharp dissection to the level of the pylorus (Fig. 1B). After the associated GSM flap based on the omental pedicle was completely dissected from the gastric mucosa, the omental leaves were divided and ligated with a 5-zero silk suture, and the flap was rotated 180° counter-clockwise for transferring to the bladder (Fig. 2A). Following harvest, the flap contracted by 15 to 20% of its initial size. After the flap was obtained, the bladder was catheterized with two 24-gauge catheters for the preaugmentation measurement of bladder capacity and end-filling pressure. One catheter was connected to the polygraph system (Nihon Kohden, Model RM-6000, Tokyo, Japan) for pressure measurement and the other was used for saline infusion into the bladder. The bladder was completely filled until an initial drop of urine was seen to exit from the urethra, and then the bladder capacity and end-filling pressure were measured [5]. After urodynamic analysis, the bladder was opened, and the GSM flap with the omental pedicle was anastomosed to the bladder with a single layer 7-zero polyglactin 910 suture (Fig. 2B). In all rats, the abdominal wall was closed with a single layer running suture of 5-zero Ethibond, as was the skin. Postoperatively the rats were returned to their cages, and given water on day 1, and standard rat chow on day 2. All animals received a trimethoprim-sulfomethaxosale suspension, which was added to the drinking water for the first week.

Post-death analyses

The rats underwent a re-laparotomy as described previously at 1 and 4 months) (Fig. 3). Urodynamic analysis was carried out for bladder capacity and end-filling pressure of the augmented bladder. The bladder with the omental pedicled GSM flap, and the dissected flap site on the stomach were removed, and then preserved in 10% formalin. The fixed tissues were embedded in paraffin then sectioned. Histological preparations were stained with hematoxylin and eosin and reviewed by two pathologists.

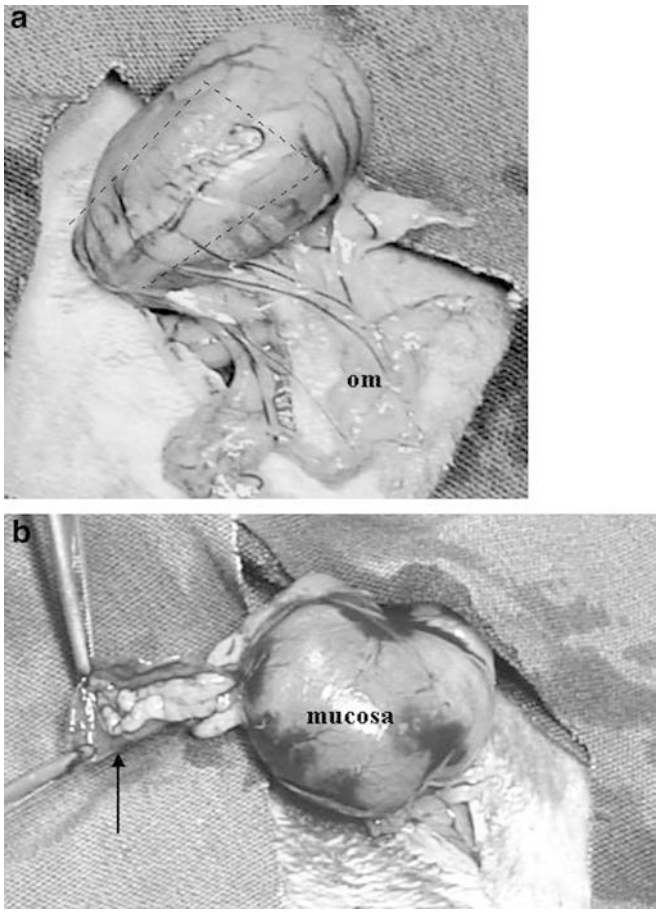

Fig. 1 **A** The incision: 10×15 mm was outlined horizontally from the region in which the collateral circulation between omental (*om*) and gastroepiploic vessels disappeared, to the pyloric antrum, and coronally from the posterior gastric surface to anterior gastric surface. **B** The flap (*arrow*) was gently separated from the gastric *mucosa* with blunt and sharp dissection

Statistical analysis

All data were expressed as means ± SD. Results were subjected to one way analysis of variance for repeat measures, and statistical significance was determined by the least significant difference (LSD) post hoc test to compare groups. In addition, the χ^2-test was used for the evaluation of the histopathological findings (SPSS 9.0 for Windows). Differences were considered significant when $P<0.05$.

Results

Four rats died because of bladder calculi and urethral obstruction during the first postoperative month. The

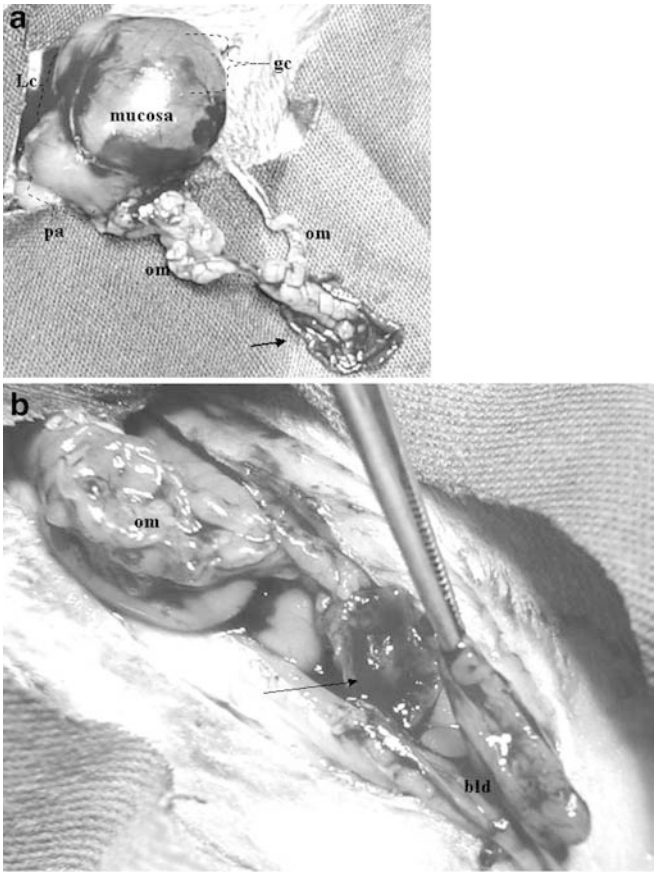

Fig. 2 **A** The flap (*arrow*) was formed by the division of the omental vessels to the mid-duodenum, and then rotated 180° counter-clockwise to allow access to the bladder. *Lc*, lesser curvature; *pa* pyloric antrum, *gc* greater curvature, om omentum. **B** The flap (*arrow*) with omental pedicle (*om*) was anastomosed to the bladder (*bld*) with a continuous suture

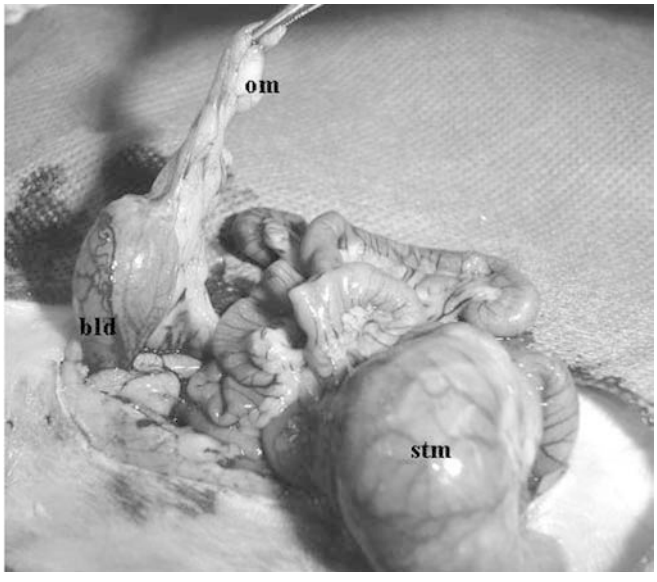

Fig. 3 At 4 months, showing the augmented bladder (*bld*) with omental pedicle (*om*) seromuscular flap, and the recovered stomach (*stm*)

mortality rate was 9% (1/11) in the 1 month rats and 21% (3/14) in 4 month rats ($P > 0.05$). All rats had macroscopic hematuria for 2–3 days postoperatively. Only one of the five rats with gross hematuria survived and had no bladder calculi. Before and after augmentation, the body weight of the rats, bladder capacity and end-filling pressure were measured (Table 1).

Body weight

All rats gained weight. Body weight significantly increased in the augmented rats compared to the preaugmentation measurements ($P < 0.05$ for 1-month rats, and $P < 0.01$ for 4-month rats). Also, the body weight of 4-month rats was significantly higher than in 1-month rats ($P < 0.01$).

Bladder capacity

Bladder capacity significantly increased in the augmented bladders compared with the preaugmentation bladders ($P < 0.001$). No significant difference was found between 1 and 4-month rats.

End-filling bladder pressure

End-filling pressures of the augmented bladders did not show any difference from the preaugmentation ones.

Histopathological findings

The histopathological results are summarized in Table 2. On macroscopic examination, there was no flap necrosis or omental torsion, and the neomucosa was completely covered the flap surface in all animals. Bladder calculi (1–3 mm in diameter) were identified in 2/10 1-month rats, and in 4/11 4-month rats. The rats with bladder calculi had increased mucosal trabeculation and debris in the bladder. Histological examination revealed that new bladder mucosa completely overlaid the muscular surface of the flap in all rats (Fig. 4A–C). Although the serosal layer of the flap could not be distinguished from the muscular layer, the omentum overlaying the flap was grossly identified. The neomucosa was characterized by varying degrees of hyperplasia and squamous metaplasia of the transitional epithelium. Epithelial hyperplasia was detected in 60% (6/10) of 1-month rats and in 55% (6/11) of 4-month rats ($P > 0.05$). One-month and 4-month rats had squamous metaplasia in 30% (3/10) and 35% (6/11), respectively ($P > 0.05$). Papilloma was identified in 50% (5/10) of 1-month rats and in 64% (7/11) of 4-month rats ($P > 0.05$). Four 1-month rats (40%) and three 4-month rats (27%) had leukocytic infiltration and inflammation of the flap ($P > 0.05$). One 1-month rat had severe

Table 1 The body weight, bladder capacity and end-filling pressure of the experimental rats (mean ± SD). Body weight significantly increased in the augmented rats compared to preaugmentation measurements, * $P < 0.05$ for 1 month group rats, and ** $P < 0.01$ for 4 month group rats). Bladder capacity significantly increased in all augmented rats compared to preaugmentation measurements, ‡$P < 0.001$

Rat group	1 month		4 months	
	Preaugmentation	After augmentation	Preaugmentation	After augmentation
Body weight (g)	170.3 ± 24.6	191.5 ± 16.6*	173.1 ± 16.3	229.09 ± 26.4**
Bladder capacity ×10 (ml)	3 ± 0.6	6.2 ± 1.07‡	2.8 ± 0.3	6.3 ± 0.9‡
End-filling pressure (mmHg)	27.5 ± 2.4	27.4 ± 3.1	25.8 ± 4.02	28.4 ± 3.9

Table 2 Summary of the histopathological findings. No significant differences were found between the 1 month and 4 month rat groups ($P > 0.05$)

	Rats at 1 month ($n = 10$)	Rats at 4 months ($n = 11$)
Re-epithelialization (neo-urothelium)	10/10 (100%)	11/11 (100%)
Hyperplasia	6/10 (60%)	6/11 (55%)
Squamous metaplasia	3/10 (30%)	6/11 (55%)
Papilloma	5/10 (50%)	7/11 (64%)
Inflammation	4/10 (40%)	3/11 (27%)
Mucosal edema	1/10 (10%)	1/11 (9%)
Microscopic calculi	5/10 (50%)	6/11 (55%)
Macroscopic calculi (1–3 mm)	2/10 (20%)	4/11 (36%)

inflammation, abscessing and erosion of the flap. Mucosal edema was seen in 1/10 of the 1-month rats and 1/11 of the 4-month rats ($P > 0.05$). Intramuscular calculi (10 of 11) and intraepithelial (1 of 11) were found in 5/10 of the 1-month rats and in 6/11 of the 4-month rats ($P > 0.05$). Only two 4-month rats with microscopic bladder calculi had gross bladder calculi.

On microscopic examination, the dissected flap surface of the stomach was completely overlaid with a new seromuscular layer in all rats.

Discussion

Reconstructive clinicians and researchers have proposed various approaches, alone or in combination, for reservoir construction and bladder augmentation [2, 6, 7, 8, 9, 10]. In the mid 1950s, Shoemaker et al. [11] compared bladder augmentation with reversed demucosalized bowel, non-reversed demucosalized bowel and conventional ileal augmentation. They suggested that reversed demucosalized bowel was the ideal tissue for bladder augmentation [1]. Although enterocystoplasty and gastrocystoplasty have been widely applied clinically since the 1960s, in recent years there have been new efforts to achieve bladder augmentation with autogenous tissues. Oesch [12] augmented the bladder with demucosalized cecum in rats, and reported viable urothelium covering the graft. Cheng et al. [13] reported that use of reversed ileal seromuscular flaps in the urinary tract in dogs resulted in good re-epithelialization of the serosal surface with transitional cells. In order to avoid direct contact between the flaps and urine, Buson et al. [14] described an initial study of seromuscular colocystoplasty lined with intact urothelium in dogs. Dewan and Byard [15] demonstrated the efficacy of a similar technique in lambs, using demucosalized stomach instead of sigmoid colon. Nguyen et al. [2] obtained a demucosalized gastric flap and applied this flap to transitional epithelium of the bladder after partial myomectomy. The disadvantage of all of these techniques using gastrointestinal segments is that gastric and bowel resection is unavoidable, and may lead to complications including ischemia and leakage of the anastomosis, organ injury, peritoneal soiling, small stomach, shortened intestine, intestinal dysmotility and an additional surgical effort. In addition, bowel epithelium was shown to re-grow, and mucocele formation appeared in the models with demucosalized bowel segments, even if the mucosa was removed by chemical and mechanical means [16].

To prevent these possible complications, we report a new procedure of bladder augmentation with a GSM flap based on an omental pedicle without gastric resection. In the literature, there are several reports of alternative techniques of augmentation cystoplasty in rat models. These do not have any significant disadvantages due to technical difficulties. Nevertheless, further studies may require the reevaluation of these models in large animals [1, 5, 17]. A flap composed of greater omentum and a full-thickness segment of the greater curvature of the stomach was first described in 1977, and proposed as a treatment for patients with bronchopleural fistulae and for use in Fournier's gangrene for urethral and scrotal reconstruction [18, 19, 20]. These flaps required continuity of the right gastroepiploic vessels. A sufficient length of the omental flap was created by ligation of the gastric rami, one by one. However, we obtained an omental pedicled GSM flap by ligation of the right gastroepiploic vessels with the preservation of the gastric rami. As the vascular connections between the omentum and gastroepiploic vessels end at the middle of the

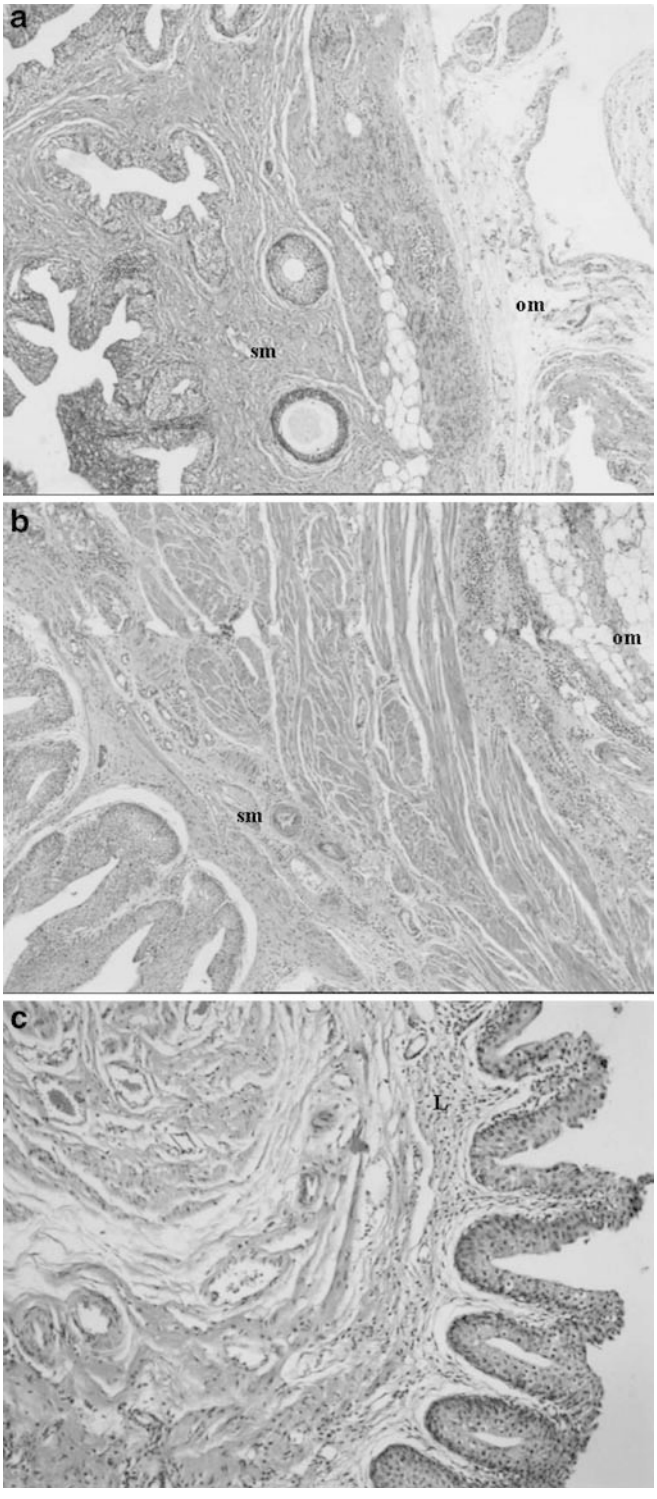

Fig. 4 Neo-urothelium completely covered the muscular surface of the flap in all rats, while normal bladder mucosa covered the lamina propria (*L*). **A** The flap at 1 month (H-E×5). **B** The flap at 4 months (H-E×5). **C** Normal bladder (H-E×10). *Om* omentum, *sm* smooth muscle

greater gastric curvature in rats, the left gastroepiploics did not require ligation. If an omental pedicled GSM flap is created in humans, several branches of the left gastroepiploic vessels, as well as the right gastroepiploic vessels, should be ligated for lengthening of the omental flap.

Some authors have suggested that augmentation cystoplasty with autogenous tissues and a demucosalized flap in direct contact with urine could not result in sufficient bladder capacity, due to severe flap contraction [1]. The technique of a demucosalized flap with vesicomyomectomy was proposed as a promising procedure for bladder augmentation. However, we have shown a net increase in bladder capacity when using an omental pedicled GSM flap in direct contact with urine. There was no significant difference in the bladder capacity and end-filling bladder pressure between augmented rats. This result demonstrates that the omental pedicled GSM flap did not produce severe contraction or reduce bladder capacity.

A variable degree of graft urothelialization may be seen with the different types of cystoplasty. Guan et al. [21] examined histopathological specimens obtained from ileocystoplasty and gastrocystoplasty in rats. Urothelialization extended from the anastomosis to the central portion of the grafts, which were only partially covered with transitional epithelium when extended over the top of the gastric or enteric mucosa. On the other hand, Aktug et al. [22] reported that the whole raw surface of the seromuscular flaps was covered with urothelium at 2 weeks after augmentation cystoplasty. Unfortunately, they observed intestinal mucosal re-growth over the seromuscular flap at 8 weeks. We found that the omental pedicled gastric seromuscular flap was completely overlaid with new urothelium, and the flap did not suffer re-growth of the gastric mucosa. This neourothelium was characterized by transitional epithelium, but also hyperplasia, squamous metaplasia and papilloma, as with other grafts. Buson et al. [23] reported an incidence of papilloma of 53.8% in gastrocystoplasty and 40.9% in sigmoid cystoplasty, and an incidence of metaplasia of 65.4% in gastrocystoplasty, 50% in sigmoid cystoplasty and 55.5% in ileocystoplasty. Demirbilek et al. [5] found hyperplasia in 12 of 13 rats with gastrocystoplasty and in five of 15 rats with seromuscular gastrocystoplasty, and squamous metaplasia in nine of 13 rats with gastrocystoplasty, and in two of 15 rats with seromuscular gastrocystoplasty. In our study, at 4 months, epithelial hyperplasia, papilloma and squamous metaplasia were found in 55%, 50% and 35% of specimens, respectively. Although the incidence of papilloma was similar to that of reported cystoplasties using other gastrointestinal segments, hyperplasia and squamous metaplasia were lower in the omental pedicled GSM flap with the except of Demirbilek's study, in which the risk of squamous metaplasia was significantly lower compared to our study. It is well known that metaplastic or hyperplastic transitional epithelium and papillary lesions are not pre-malignant. However it is possible that these abnormalities may be transformed into carcinoma by concomitant risk factors, including chronic inflammation, multiple

operations, recurrent bacterial infections and poor drainage of the bladder [24]. Thus, prevention of the risk factors should not be overlooked following bladder augmentation.

Another potential complication in bladder augmentation with a gastrointestinal segment is the risk of calculi formation, with a reported incidence of 10–50% [24]. We detected macroscopic bladder calculi in ten of 25 rats, and microscopic calculi in 11 of 21 rats (because four of 25 rats died prior to analysis due to bladder stone and urethral obstruction). As only two rats with microscopic calculi had gross calculi, there appeared to be no correlation between microscopic and macroscopic calculi formation The etiology of stones in the augmented bladders is unclear, and has been explained by other authors as due to several predisposing factors including metabolic abnormalities, infection, foreign body reaction, stasis and mucus production. Khoury et al. [26] suggested that mucus played an important role in calculi formation, possibly acting as a nidus. Although the omental pedicled GSM flap, as well as other seromuscular flaps, do not have mucus production, the rats with seromuscular cystoplasty developed bladder stone. This result suggests that risk factors other than mucus production also play a significant role in calculi formation.

In conclusion, the omental pedicled GSM flap offers the obvious advantages of a vascular flap for augmentation without a full-thickness gastric or intestinal resection, as well as tension-free mobilization on an omental pedicle limited by omental mobility. This may be considered as an alternative technique for experimental bladder augmentation. However, these very early results will need to be studied to further eliminate the significant problems of calculi formation and inflammation, and further studies are planned using variants of auto-augmentation in which the omental pedicled GSM flap is anastomosed to naked bladder mucosa to avoid the risk factors due to direct contact of the flap with urine.

Acknowledgment This study was supported by Akdeniz University Management Unit of Scientific Research Projects.

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