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UROLOGY - REVIEW

Bladder augmentation from an insider's perspective: a review of the literature on microcirculatory studies

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Abstract
Augmentation cystoplasty is an exemplary multiorgan intervention in urology which is particularly associated with microvascular damage. Our aim was to review the available intravital imaging techniques and data obtained from clinical and experimental microcirculatory studies involving the most important donor organs applied in bladder augmentation. Although numerous direct or indirect methods are available to assess the condition of microvessels the implementation of microcirculatory diagnostic methods in humans is still challenging and the assessment of organ microcirculation in the operating theatre has limitations. Nevertheless, preclinical studies generally report good internal validity and although prospective human protocols with reduced variability are needed, a possible positive impact of microcirculatory diagnostics on the clinical outcomes of urologic surgery can be anticipated.

Keywords Bladder augmentation · Microcirculation · Blood perfusion · In-vivo microscopy · Gastrointestinal flap · Reconstructive surgery

Introduction

Compromised circulation can lead to acute wound healing failures or anastomosis disruption with the leakage of intraluminal contents. Chronic or unrecognised ischemia may be present in the background of late spontaneous perforation, graft fibrosis or shrinkage. To prevent these complications, surgeons have learned to respect the rules of macroscopic vascular anatomy during incisions or tissue mobilisation. Nevertheless, the visible arterial and venous parts of the circulatory system are linked by the microvessel network, and, as a result of technical developments, considerable knowledge has also been accumulated on the intramural microcirculation of the organs. These imaging modalities can help surgeons and researchers to realise the limitations of surgery and improve techniques and thus reduce the risk of postoperative complications.

Our main goal was to prepare a comprehensive literature review on the role of the microcirculation of the most important donor organs (the small intestine, colon and stomach) in the success of bladder augmentation (enterocystoplasty) or related complications and evaluate the possible impact of preclinical research on clinical practice. We included clinical and experimental studies published between 1 January 1997 and 1 October 2020. The PubMed database was searched on 1 October 2020 with the following keywords and multiple combinations: stomach, small intestine, colon, urinary bladder, bladder augmentation, bladder enlargement, microcirculation, microperfusion, capillary function, capillary density, microvascular flow and blood flow. The relevant studies were summarised according to their set-up (clinical study or animal experiment), organ type and outcomes. In the case of multiple publications, the authors considered the latest articles to be included in the review.

Enterocystoplasty (bladder augmentation using bowel segments)

Decreased bladder capacity, high intravesical pressure and low compliance are main indications, with the goal of

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providing a low-pressure reservoir and preserving upper urinary tract function and patients' continence [1]. At present, enterocystoplasty is the most favoured method, while other procedures, such as auto-augmentation of the detrusor muscle, are less common. Many parts of the gastrointestinal (GI) tract can be used for bladder enlargement, but the preferred organ is the ileum [1]. Although augmentation is a routine procedure, complication rates are high and anastomotic leakage occurs in 6–24% of cases [1–6]. Early perforation is usually located on the suture line, while late perforation involves the augmented bowel segment, somewhat farther from the anastomosis line [5]. A higher perforation rate has been reported after colocystoplasty [6, 7]. Many reasons and factors, such as intravesical overpressure, transmural infection, intraperitoneal adhesions and obstruction by mucus, are recognised, but the exact pathophysiology is often unknown [6, 8–11]. In these cases, the critical role of insufficient microcirculation is generally assumed, but not proven, mostly due to technical limitations, which are summarised below.

Microcirculation of the urinary bladder

Ample data is available on the microvascular structure of the human and animal bladder [12, 13], but studies on ischemia–reperfusion injury do not focus on clinical consequences. The bladder is a dynamic organ, with storage function secured by volume changes and structural mobility and by blood flow and microcirculation changes during the filling and emptying phases [12–14]. The human bladder is nourished by one or two cranial and one or two caudal vesicular arteries from both sides [13]. The bladder wall is well vascularized, but the capillary density can be distinctively different in layers [12]. This system is adapted to dynamic changes with an excessive folding and coiling mechanism and extreme tortuosity of vessels. A vasculature break is obvious at the submucosa; in addition, the vasculature of this layer is poor, and there are only a few essential vascular interconnections between the mucosa and muscular layer [12]. The loose connective tissue is associated with the submucosa and provides free movement of the mucosa. Vessel plexuses come close to the mucosal surface from the lamina propria and lie perpendicular to the surface; hence, they can move apart laterally without tension. Arterial sphincter and venous valves are frequent; they probably aid in controlling continuous blood flow during intraluminal pressure changes, and the rich collateral system also supports favourable haemodynamic outcomes [12]. However, there are no exact measurements; there is only empirical experience available in this area.

Therefore, we can reasonably assume that the arrangement of the bladder wall vessels should make it possible to maintain blood flow during normal filling; however, circulation in the bladder wall could suffer serious changes in conditions where intravesical pressure reaches certain limits for a certain time (neuropathic bladder, subvesical obstruction caused by the posterior urethral valve, obstructive ureterocele, overactive bladder and dysfunctional voiding) [8, 15]. Other conditions, such as ageing-related arteriosclerosis, can also lead to chronic bladder ischemia [16].

The main problem in microcirculatory impairment (chronic ischemia) seems to be leukocyte adherence to the endothelium. Significant microcirculatory damage and an increase in leukocyte and lymphocyte infiltration have been observed after ischemia in rats [8, 16]. In parallel, venular red blood cell velocity and functional capillary density (FCD) decreased to 36% and 28%, respectively, and small vessel diameters fell to 73% compared to the control group. The main factors of this phenomenon are hypoxia and reoxygenation, which jointly initiate inflammatory processes with "no-reflow" and "reflow paradox" phases. Cell swelling and leukocyte entrapment exacerbate tissue hypoxia, while metabolic energy impairment and production of reactive oxygen species contribute to tissue injury during reperfusion. This process is finally presented in structural and functional changes, such as denervation or detrusor overactivity, which develops into underactivity [16]. The degree of damage depends on the duration of the ischemic episode.

Microcirculation of the primary GI donor organs for bladder augmentation

Gastric tissue

Gastrocystoplasty provides an alternative for children with chronic renal failure and azotemia or short bowel disease. It has no severe effect on the acid–base equilibrium in contrast to the ileum or colon tissues, both of which can cause metabolic alkalosis. Moreover, less mucus production and acidic urine reduce the infection rate (Fig. 1). Nonetheless, gastrocystoplasty significantly increases the number of malignancies; the technique has thus very rarely been indicated [1, 2].

More microcirculatory data are available on gastric tube formations during esophagectomy [17–22]. During the mobilisation of the stomach pedicle flaps, the left and/or right gastric arteries, the left gastroepiploic artery and some of the short gastric arteries are ligated [18], causing radical microcirculatory changes [17, 19]. At least one artery out of these four—the right gastroepiploic artery—must be spared to supply the gastric tube. The right gastric artery is also preserved, but its importance is negligible. The decrease in blood flow can lead to ischemia, and a number of animal experiments and human studies have also confirmed that the fundus is the most affected area. Of note, the highest frequency of anastomotic leakage has been described in this

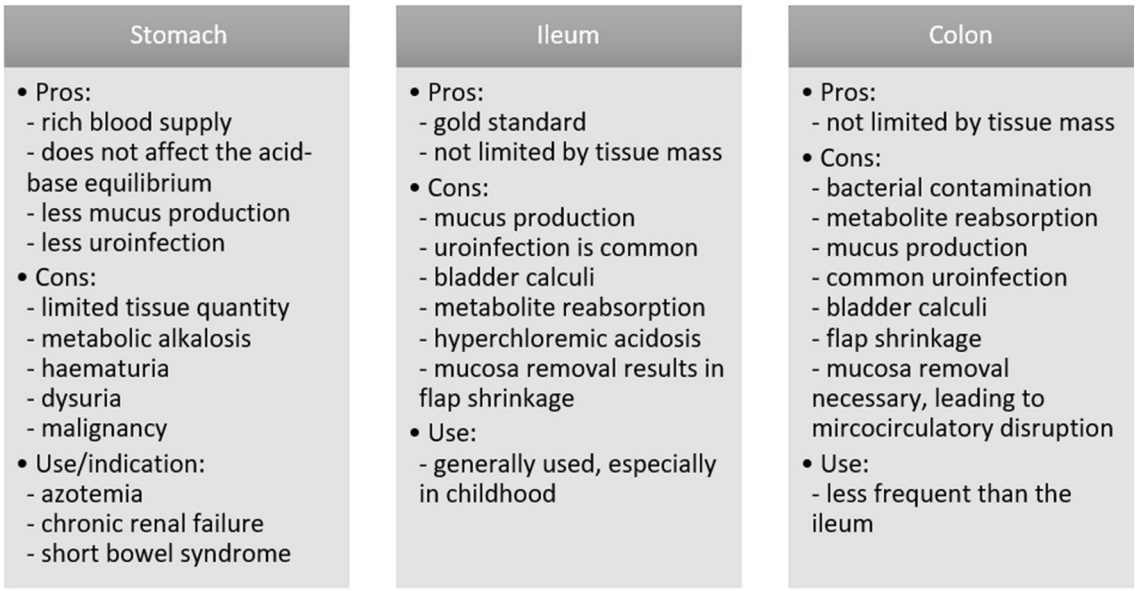

Fig. 1 Comparison of gastrointestinal segments for bladder augmentation

region. The first pioneering studies documented the changes of FCD in a rat model during an eight-week period [23, 24]. An immediate, approx. 55% reduction was measured on the lesser curve and a 16% decrease on the greater curve. After 4 weeks, the FCD of both regions significantly improved and by the eighth week, the values measured at the lesser curve also reached the range of the normal values. After the gastric conduit formation, the parameters also fell significantly in the corpus and fundus. During esophagectomy, the gastric pull-up step also increased the anastomotic failure rate in 42% of animal models [25]. These models help to analyse the microcirculatory alterations and anatomical differences between humans and animals, which are considerable [26]. For instance, the left gastric artery is dominant in humans, while it is the left gastroepiploic artery that is more significant in pigs.

In an open Ivor–Lewis esophagectomy, a 25% decline in perfusion was detected in the fundus and corpus during mobilisation [27]. The parameters of the antrum did not change. After the pull-up step, there was an additional drop in affected areas, so the total decrease was 40%. In laparoscopic gastrolysis, a significant decline in mucosal oxygen saturation was documented from 72 to 38% in the fundus, which returned to 62% 5 five days later [28].

Delko et al. [29] examined the intraoperative microvascular consequences of laparoscopic sleeve gastrectomy in 20 patients. During sleeve gastrectomy, the greater curvature and vascular arcade were resected; that is, the gastroepiploic arteries were dissected. Tissue oxygen saturation was measured in nine zones in three phases: before and after mobilisation, and during resection. In phase I the uppermost part of the greater curvature had the lowest saturation by 56%. This value was higher (49%) in this zone after phase II. After resection, the lowest saturation by 49% was identified close to the esophagogastric junction and resection line. This study also shows that the fundus has the lowest perfused part of the stomach as it does during esophagectomy.

The small intestine

The clam ileocystoplasty is the most popular and widespread method of bladder augmentation, especially among children [30]. The main steps are mobilisation of the ileum, detubularisation and bladder augmentation. An intact, reliably perfused vascular pedicle without any significant tension is crucial for the proper fitting of the ileal flap to the bottom of the divided bladder (Fig. 1). Certain conditions, like inflammation, peritoneal dialysis and ventriculo-peritoneal shunts, or previous surgery can cause the shortening of the ileal mesentery. An experimental study was conducted on the use of an alternative ileum detubularisation [30]. An alternative incision close to the mesentery was used to detubularise the ileum in one group, while in the control group the incision was made on the antimesenteric line. Additionally, this was combined with ligation of a different number of vasa recta. Alteration was not detected in capillary red blood cell velocity or in the perfusion rate in groups without ligation of the vasa recta. Ligation of one vessel did not affect microcirculation, but a reduced microperfusion was detected for the ligation of two or more vessels. Nonetheless, after ligation of four vasa recta, a largely decreased but still detectable microcirculation was present. Paramesenteric

detubularisation resulted in a significantly longer flap than in the control group. Therefore, the authors recommended the dissection of vessels at the level of the primary, secondary and tertiary arcades of the mesentery to create an adequately long pedicle for the ileum flap [30].

Further, there have been several attempts at preventing mucus secretion [31–33]. Cerveillone et al. studied the changes in microcirculation after mucosectomy and the phenomenon of flap shrinkage in pigs. In the first group, mechanical scraping was used to eliminate the mucosa, while they peeled off the mucosa and submucosa in one layer in the second group. A significant reduction of serosal microcirculation was observed in both groups. The study also investigated the role of omentopexy during augmentation, which is an accepted method to facilitate revascularization in numerous organs, such as the trachea, myocardium and brain; however, no evidence was found for its effectiveness in ileocystoplasty [33].

Spontaneous bladder perforation after enterocystoplasty is a well-known serious complication after ileocystoplasty. It has been explained by iatrogenic trauma caused by the catheter during intermittent catheterisation and decreased sensation, chronic infections and overextension with failed catheterisation. A rat model experiment compared the microcirculatory effect of the intravesical pressure and chronic overpressure on the bladder wall and the ileum after enterocystoplasty and demonstrated the limits of the ileum for bladder augmentation [8]. In these controlled circumstances, there was no significant microcirculatory difference between the intact bladder, augmented bladder and intact intestinal segment when 20 mmHg intravesical pressure was applied for 60 min. The mean closure pressure of the urethral sphincter was similar. Over 25 mmHg pressure, red blood cell velocity decreased about 50% in the augmented bowel. At 40 mmHg intraluminal pressure, almost complete stasis was observed; however, in an intact bladder, the first changes in blood cell velocity were registered from 80 mmHg. Moreover, the capillary perfusion rate was similar, although the baseline value at the bowel was higher than that of the bladder. The higher baseline value may be explained by the larger capillary density of the bowel than that of the bladder. The authors concluded that the relatively low pressure tolerance of the ileum within the augmented bladder should be considered during ileocystoplasty when the augmented bladder is designed to avoid spontaneous perforation. Further, the rat model is capable of differentiating acute and chronic adaptive responses [8].

The colon

The sigmoid colon with its long, easily accessible mesentery remains a good option for bladder augmentation; however, the higher amplitude contractions and mucus production make it less favourable than the ileum (Fig. 1).

Far more less studies are available regarding the microcirculation of the colon than the small intestine. They rather focus on colorectal surgery-induced consequences, but their summary is valuable. Tavy et al. measured both the serosal and mucosal microcirculation during surgical manipulation in humans [34]. Anastomosis or stoma was conducted by laparoscopic or open surgery to prove that the mucosal microcirculation is more vulnerable than the serosal microcirculation. During the operation, the mucosal perfusion was more stable; however, the serosal baseline value was significantly lower than the mucosal one. The difference in vessel density between the two surfaces may be explained by anatomical specificity. The serosal microcirculation was significantly lower during laparoscopy than open surgery; however, this does not correlate with clinical outcomes [34]. Moreover, a comparative study demonstrates significantly lower anastomotic insufficiency after laparoscopic colorectal surgery [35].

Other researchers have investigated microcirculatory alterations on the serosal layer because anastomotic leakage occurs in 3–19% of colorectal surgeries [36]. The microcirculation was measured at the anastomotic line and 15–20 cm from there in the oral direction. Significantly lower perfusion was detected on the resection line. The reduced perfusion could correlate with an anastomotic healing problem; however, they also highlighted that not all vascular abnormalities lead to anastomotic failure [34, 37]. In addition, visual control by surgeons has a low predictive factor in detecting optional microcirculatory insufficiency.

In ischemic conditions, the colonic serosa was more compromised than the mucosal circulation [38]. The use of intraoperative ICG to examine the microcirculation of the resection line could significantly reduce the rate of anastomotic leakage [33, 39]. However, an intraoperative analysis of the microcirculation is a subjective procedure, and the ICG technique could be biased due to the capillary flow diffusion [37].

Intramucosal pH was detected close to the anastomoses in the first 24 h and 48 h periods after colon resection in 90 patients. Leakage developed in 6.6%, and the risk of leakage was 22 times higher if the intramucosal pH was less than 7.28 in the first 24 h [40]. Other authors used an alternative approach to find a correlation among the intra- and postoperative microcirculatory findings in a rat model and only the postoperative microcirculatory values showed a significant correlation with the anastomotic bursting pressure. Therefore, a longer postoperative follow-up for microcirculatory diagnostics is called for [41].

As noted previously, mucus related complications are more severe after colocystoplasty. To prevent them, mucosectomy seem to be a promising alternative. An experimental

study showed successful transplantation of cultured urothelium to the sigmoid colon after mucosectomy [42]. Successful experimental augmentation was reported with composite bowel and no shrinkage of the composite flaps. However, looking closer into the study we found three pigs were lost due to sepsis secondary to urine leakage at the early postoperative period, two additional pigs were lost because of urine leakage from the anastomotic line, one graft showed shrinkage among the seven surviving. Others failed to reproduce similar results with demucosalised reverse ileum flap [32]. Flap shrinkage was detected and significantly decreasing microcirculatory parameters also occurred in all animals with reversed ileal flap [32]. However, they did not lose animals due to urine leak, but all flaps contracted significantly. The authors blamed the impaired microcirculation measured with OPS on the demucosalised ileum segments. It may be argued the responsibility of the reverse technique, however, in one animal where mucosectomy was not performed (control) the flap remained intact with the reverse technique. Another study showed damaged enteric nervous system after mucosectomy assuming this may contribute to shrinkage as well [33].

It is not obvious, but structural differences between small intestine and colon might explain these different experiences. Further studies are necessary to clarify the effect of mucosectomy on colonic segments.

Microvascular diagnostics

Intact microvascular flow is recognised as a primary factor in the healing of GI anastomoses; there is therefore a high demand for reliable, easy-to-use intra- or postoperative diagnosis. Not surprisingly, a wide range of clinically available methods have been developed and tested with variable success (Table 1 and Fig. 2). Devices with laser Doppler flowmetry (LDF) can measure red blood cell velocities endoscopically in the mucosal microcirculation [43]. Simple and non-invasive, LDF is capable of real-time detection; however, it uses arbitrary units like the majority of other optical techniques, and zero-point calibration is missing. The evaluation requires experience because of the heterogeneity and overlay of vessels [34, 43]. It is therefore not recommended as a first choice in intraoperative measurements. Laser speckle contrast imaging (LSCI) also provides arbitrary units and colour-coded images [43]. Although it is more sensitive than LDF and has fewer artefacts, the clinical feasibility of LSCI has not been confirmed.

Fluorescence imaging (FI) has gained renewed popularity in recent years. Here a laser beam illuminates the tissue, where a fluorescent molecule is activated [43]. The quality of perfusion is usually assessed with indocyanine green (ICG), and this technique may predict the potential of anastomotic necrosis intraoperatively. However, quantitative parameters

Table 1 Summary of available microcirculation measurement techniques in clinical and experimental surgery

Authors (reference number)	Year	Study design	Patient/elementnumber	Optical technique	Target organ	Outcome	Dye
Akiyama et al. [37]	1996	Human	79	LDF	Stomach	QUP	No
Schilling et al. [44]	1997	Pig	36	LDF	Stomach	QUP	No
Schröder et al. [27]	2002	Pig	17	LDF	Stomach	QUP	No
				Tonometry		QP	
Schröder et al. [28]	2004	Human	49	LDF	Stomach	QUP	No
				Tonometry		QP	
Ambrus et al. [45]	2017	Human	25	LSCI	Stomach	QUP	No
Prasetya et al. [41]	2018	Artificial	1	FI	Stomach	QUP	ICG
Wada et al. [52]	2017	Human	112	FI	Colon	QUP	ICG
Jafari et al. [55]	2013	Human	22	FI	Colon	QUP	ICG
Cserni et al. [47]	2015	Pig	5	OPS	Small intestine	QP	No
Cerveillone et al. [48]	2016	Pig	6	OPS	Small intestine	QP	No
Siegemund et al. [54]	2010	Pig	15	OPS	Colon	QP	No
				Tonometry		QP	
Bajory et al. [8]	2001	Rat	50	IVM	Bladder	QP	ITC
Mittermair et al. [43]	2008	Rat	20	IVM	Stomach	QP	ITC
de Bruin et al. [51]	2018	Human	10	SDF	Colon	QP	No
Tavy et al. [13]	2020	Human	9	IDF	Colon	QP	No
Millan et al. [56]	2006	Human	90	Tonometry	Colon	QP	No

QUP qualitative parameter with arbitrary units, *QP* quantitative parameter, *ITC* isothiocyanate, *IVM* intravital microscope

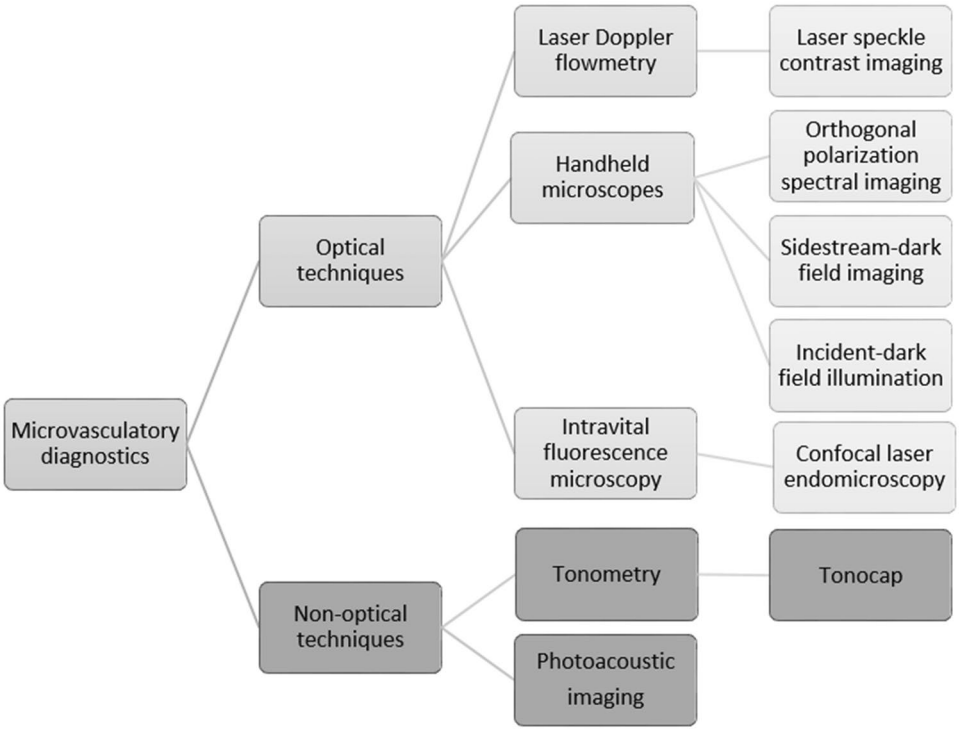

Fig. 2 Groups by microcirculation measurement technique

have not yet been described [43]. Moreover, images taken with this technique could be overestimated because ICG molecules can infiltrate the congested tissue to some extent simply by diffusion from the healthy zone [44].

Confocal laser endomicroscopy (CLE) is based on the principles of intravital fluorescence microscopy combined with optical fibres. With the added value of confocality, fluorescence imaging can evaluate functional capillary density, blood cell velocity, changes in permeability, vasoconstriction and dilation [45]. Confocal images can provide information not just on the microcirculation, but also on the morphology of intestinal villi and crypts [46, 47]. Fluorescein isothiocyanate–dextran enables us to see the capillary system, while acridine orange dye shows epithelial loss, which may be crucial to determining viability at the resection line. Moreover, CLE is successfully used for an "optical biopsy" to conduct a morphological analysis for ulcerative colitis and removal of tumour tissue [48–51]. In fact, CLE might be a reliable asset for diagnostics, with limited invasiveness, ease of use and preservation of the physiology of the organ being great advantages.

Orthogonal polarisation spectral (OPS) imaging was used by the first generation of handheld microscopes, which were able to directly visualise human microcirculation without contrast materials [52]. It is still appropriate for intraoperative measurement, but image stabilisation is difficult. Sidestream dark field imaging (SDF) illuminates the tissue with green LED light with higher resolution, but it still requires direct contact with the tissue [3]. In addition, movements, such as heartbeat, compression and breathing, may distort results [43]. Incident-dark field illumination (IDF) was the next generation of handheld devices; it was completely digital and showed a significantly higher rate of total vessel density [53]. Moreover, it has a shortened pulse time, a digital stabiliser and reduced weight. In brief, OPS, SDF and IDF can all measure the important parameters of microvascular flow, including total vessel density, the proportion of perfused vessels and the flow heterogeneity index, as recommended by a roundtable consensus meeting on this subject [54].

A more recent technology in the preclinical phase is photoacoustic imaging (PAI). Pulses of non-ionising laser light are absorbed by tissues, and the heat, which is caused by energy absorption, results in a thermoelastic expansion [55]. The accompanying sound effect can be detected by high-sensitivity ultrasonic transducers. Haemoglobin- and melanin-containing tissues can be effectively examined with this method. The intravascular lumen contains a significantly larger amount of haemoglobin than surrounding tissues; therefore, no contrast agent is necessary to investigate the microvascular system [55]. Clinical testing is promising because of three-dimensional visualisation and the possibility of simultaneous analysis of tissue morphology and the vascular system. The main limitations of this technique are that a handheld version is currently unavailable and greater penetration depths are necessary. However, PAI endoscopy is a promising solution for intra- and postoperative follow-up [56].

Tonometry has changed over time. Modern devices with infrared sensors, calibrations and automatically sampled gases can detect the partial pressure of carbon dioxide (pCO_2) and calculate intramucosal pH. Studies have confirmed the predictive potential of mucosal pCO_2 in septic and critically ill patients and intra- and postoperative monitoring [26, 57]. Indeed, the levels of mucosal oxygen and CO_2 saturation are clinically relevant parameters of microcirculation in humans [28, 58]. Mucosal pCO_2 detection is appropriate for intraoperative control of microcirculation and capable of continuous postoperative monitoring after oesophagectomy or other surgery [57]. Easy clinical application and the possibility for long-term monitoring during the postoperative period in intensive care units also represent advantages.

Discussion and summary

Operative techniques have been refined significantly, but the rate of anastomosis complications is still high. There is therefore an effort now to understand the pathophysiology better. The tradition of an expert surgeon being able to evaluate tissue viability with the naked eye persists; however, its inaccuracy is increasingly evident. Surgical manipulation critically affects tissue microperfusion, and, unsurprisingly, a growing body of experimental data has resulted in more attention on the human microcirculation. The current knowledge of the microcirculation of organs during enterocystoplasty is heterogeneous and limited, but certain conclusions can be considered. For instance, the stomach has been well studied to improve the oesophagectomy technique, and development efforts in colorectal surgery show a very similar picture. GI complications are mostly based on ignorance of the role of the microcirculation in tissue regeneration, and, therefore, an examination of microperfusion with the latest technical improvements could be expanded to include urological practice.

The stomach would be an ideal source for bladder augmentation from the perspective of the tissue microcirculation. Its durability and rich microcirculation would be conducive to bladder augmentation; however, because of the metabolic complications, it has recently only been used in selected patients who suffer from bowel irradiation, short bowel syndrome or cloacal exstrophy. The dense vascular system can compensate for lack of the right gastroepiploic artery, which is used for the gastric flap via transmural plexuses, and it does not affect the sensitive microcirculation of the fundus. Further, the resected corporeal flap has a strong arterial supply. Unfortunately, venous congestion may adversely impact the microcirculation. Super discharge and "bloodletting" techniques have also been used to resolve this issue, although there is no data on the effectiveness and their effect on the microcirculation is only empirical.

Ileocystoplasty is used as the current gold standard for augmentation. Various surgical manipulations, such as antimesenteric detubularisation and spiral lengthening, are well tolerated by the ileum [29, 30]. However, the implanted ileal flap shows deteriorating microcirculation values and leukocyte activation under chronic high intravesical pressure, leading to ischemia and resulting in perforation [8]. A mucosa also generates numerous metabolic and infectious problems; mucosa removal is required to prevent these complications.

Nevertheless, the mucosal layer is key to the vascular regulation of the bowel wall, and the serosal layer is more sensitive to microcirculatory changes [34]. Indeed, mucosectomy adversely impacts microcirculatory function [30]. A complete mucosectomy requires removal of the submucosal layer. Its role in flap shrinkage cannot be ruled out [31]. Further studies are required to understand the complex changes in the regulation and distribution of the microcirculation during surgical manipulation of the colon and small intestine, as with mucosectomy, to prevent mucosa-linked complications. It is also important to ascertain exactly how regulation of the microcirculation between the serosal and mucosal layers works. Another key factor is the enteric nervous system. We have previously highlighted the potential role of disrupted neuronal links between the submucosal and myenteric plexuses in flap shrinkage after mucosectomy [31]. A deeper understanding of the pathophysiology in the background of long-term changes in the microcirculation of the augmented bowel flap may lead to an improved enterocystoplasty technique by reducing the prevalence of anastomotic leakage and other long-term microperfusion-related complications.

The importance of real-time, dynamic examination of microperfusion is increasingly evident. Nonetheless, no available method is devoid of compromises. LDF, LSCI and IF are not recommended because they use arbitrary units which are difficult to interpret [54]. No laparoscopic or endoscopic versions of OPS, IDF or SDF exist, a disadvantage for minimally invasive surgery. CLE may incorporate a number of advantages of previous devices, such as quantitative parameters, real-time visualisation and the option of optical biopsy. Today it seems CLE can resolve the intra- and postoperative difficulties of microcirculation measurements in urological use. CLE may be appropriate for long-term follow-up, and morphological analysis may be suited to checking inflammation and malignant transformation. Furthermore, it is important to clarify the role of transmural plexuses, the regulation of sero-mucosal microcirculation, and high intravesical pressure-induced ischemia. Microcirculatory investigative methods are now available, and postoperative follow-up is possible. Long-term enterocystoplasty

experiments and prospective clinical studies are thus necessary to understand and improve the pathology of these conditions.

We have learned so far that the vascular and neural integrity of the donor tissue used for bladder augmentation is crucial to uneventful healing. We are convinced that the current popular research trend of creating a composite bladder with a mucosal replacement after a mucosectomy of the ileum and colon is a cul-de-sac. The stomach might have some reserves. Donor organs may be replaced in the future with artificial tissue; however, for a long-term sufficient result (without a long-term contraction), the microvascular blood supply to this new tissue needs to be safely and adequately provided. Research should focus on (micro)vascularised scaffolds first. In this line of reasoning, techniques for monitoring and assessing the microcirculation represent a highly innovative area which will play an important role in the development of urologic surgeries.

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