

# Liberal versus Modified Intraoperative Fluid Management in Abdominal-flap Breast Reconstructions. A Clinical Study

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**Background:** The outcome of reconstructive microsurgery is influenced by the intraoperative anesthetic regimen. The aim of this study was to compare the impact on the intra- and postoperative complication rates of our modified fluid management (MFM) protocol with a previously used liberal fluid management protocol in abdominal-flap breast reconstructions.

**Methods:** This retrospective study analyzed adverse events related to secondary unilateral abdominal-flap breast reconstructions in two patient cohorts, one with a liberal fluid management protocol and one with a MFM protocol. In the MFM protocol, intravenous fluid resuscitation was restricted and colloid use was minimized. Both noradrenaline and propofol were implemented as standard in the MFM protocol. The primary endpoints were surgical and medical complications, as observed intraoperatively or postoperatively, during or shortly after the hospital stay.

**Results:** Of the 214 patients included in the study, 172 patients followed the MFM protocol. Prior radiotherapy was more frequent in the MFM protocol. Surgical procedures to achieve venous superdrainage were more often used in the MFM cohort. Intraoperative as well as postoperative complications occurred significantly more frequently in the liberal fluid management cohort and were specifically associated with partial and total flap failures. Prior radiotherapy, additional venous drainage, or choice of inhalation agent did not have an observable impact on outcome.

**Conclusions:** The incidence of adverse events during and after autologous breast reconstructive procedures was reduced with the introduction of an MFM protocol. Strict intraoperative fluid control combined with norepinephrine and propofol was both beneficial and safe. (*Plast Reconstr Surg Glob Open* 2021;9:e3830; doi: 10.1097/GOX.0000000000003830; Published online 17 September 2021.)

## INTRODUCTION

The anesthetic goals in flap surgery are to provide optimal tissue perfusion and oxygenation.<sup>1</sup> Intraoperative hypotension is a well-known risk for postoperative complications and is commonly counteracted by intravenous crystalloid infusion.<sup>2,3</sup> Intravenous colloids can provide additional support to prevent hypotension.<sup>4</sup> Besides normal insensible water loss and urine production, there is a

constant physiological fluid transfer from the intravascular to the interstitial compartment.<sup>5</sup> Ischemia-reperfusion injury (IRI) can induce increased capillary leakage, leading to excessive fluid entrapment in the tissue.<sup>6</sup> Superfluous intraoperative fluid resuscitation causes interstitial fluid overload and results in an increased risk for complications.<sup>4,7,8</sup>

Vasopressors can be used to maintain adequate blood pressure and reduce the need for additional fluid infusion. In reconstructive microsurgery, there has been skepticism toward using vasoactive agents due to concern of vasospasm and reduced flap perfusion.<sup>9</sup>

Inspired by studies on restrictive fluid administration in elective gastrointestinal surgery, we introduced in 2005 a modified fluid management (MFM) protocol in abdominal-flap breast reconstructions, aiming to reduce intraoperative fluid volumes and complications.<sup>10</sup> Vasopressors were used liberally to maintain normotension, and propofol (Propofol-Lipuro, B. Braun, Melsungen AG, Germany) was introduced to minimize the impact of

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IRI.<sup>11</sup> The aim of this study was to compare the impact of our MFM protocol with a previously used liberal fluid management (LFM) protocol on intra- and postoperative complications in secondary unilateral abdominal-flap breast reconstructions.

### PATIENTS

This retrospective study included patients scheduled for secondary unilateral abdominal-flap breast reconstruction over a period of 20 years (1999–2018). The study was approved by the regional ethical committee and accomplished in accordance with the Helsinki declaration. Patients were allocated to two cohorts, corresponding to which of the two protocols was followed. The MFM protocol was fully implemented in 2005, which therefore served as a dividing time-point between cohorts. Exclusion criteria were patients with obstructive pulmonary disease, coronary artery disease, peripheral arterial disease, or use of nicotine products within three months before admission. A complete anesthesia record was mandatory.

### METHODS

#### The Liberal Fluid Management Protocol

The LFM comprised isoflurane or sevoflurane inhalation anesthesia at the discretion of the anesthesiologist. Crystalloids were used to maintain normotension (mean arterial pressure  $\geq$  65 mm Hg). Intravenous colloids were added on demand to correct hypotension irresponsive to increased crystalloid fluid infusion. Vasopressors were occasionally utilized to correct hypotension, unless manageable with intravenous fluids and colloids.

#### The Modified Fluid Management Protocol

The MFM comprised sevoflurane as the predominant inhalation anesthetic. Crystalloids combined with vasoactive agents were used to maintain mean arterial pressure of 65 mm Hg or greater. Colloids were used very restrictively and only to correct hypotension irresponsive to boluses of norepinephrine and crystalloids. Inhalation anesthesia was replaced by propofol infusion after completion of the microvascular anastomoses.

#### Surgical Treatment and Follow-up

Pedicled transverse rectus abdominis musculocutaneous flaps were performed by a single team, whereas free flap surgery was accomplished by a two-team approach using the internal mammary vessels as the preferred recipient vessels. Venous superdrainage was performed if venous congestion was suspected, based on intraoperative assessment by infrared thermography and clinical signs.

Hemoglobin and hematocrit levels were measured preoperatively and 1 and 2 hours postoperatively. Postoperative flap monitoring was accomplished by handheld Doppler ultrasound and clinical evaluation every hour until 24 hours after surgery, and thereafter every two hours until postoperative day 3 and every 6 hours until discharge. Hypotensive episodes were defined as mean arterial pressure less than 65 mm Hg. Relevant surgical and medical information was obtained from the patient records.

Primary endpoints were surgical and medical complications (Table 1). Postoperative complications were registered during hospital stay and until 2 weeks after discharge. Wound infection was diagnosed based on local and systemic clinical signs, and/or unexplained rise in inflammatory markers (CRP, WBC).

#### Statistical Analysis

Differences between cohorts were determined using chi-Square or Fisher’s exact tests (FET) for binominal categorical variables and independent sample *t*-test for normally distributed ordinal continuous variables. Significantly different variables were included in a multivariate logistic regression model to assess independent association with outcome. Data were analyzed using SPSS statistical software (IBM Corp. IBM SPSS Statistics for Windows, Version 25.0., Armonk, N.Y.). Statistical significance was defined as a *P* value less than 0.05.

### RESULTS

The LFM cohort contained 42 patients, and the MFM cohort, 172 patients. There were no significant differences between cohorts regarding age or body mass index (Table 2). Prior radiotherapy was more frequent in the MFM cohort (*P* < 0.05).

#### Anesthesia and Medical Treatment

The anesthesiologic results are summarized in Tables 3 and 4. Sevoflurane was the most common anesthetic agent in both cohorts. Propofol was much more frequent in the MFM cohort, as expected (*P* < 0.05).

Intraoperatively, the LMF cohort received more fluid but had lower urine output. The end-surgery fluid accumulation in the LFM cohort was  $53.8 \pm 22.0$  ml/kg

**Table 1. Assessed Complications by Category**

Intraoperative Complications	Postoperative Surgical Complications	Postoperative Medical Complications
Bleeding > 500 ml	Bleeding > 500 ml	Cardiac arrhythmia
Inadequate flow in recipient artery on surgical exploration	Wound infection	Congestive heart failure
Arterial anastomotic thrombosis	Wound rupture	Myocardial infarction
Venous congestion	Partial flap loss	Pulmonary embolism
	Total flap loss	Deep vein thrombosis
	Hernia at abdominal donor site	Acute renal failure
		Respiratory distress
		Urinary tract infection

**Table 2. Patient and Case Characteristics**

	LFM Protocol (n = 42)	MFM Protocol (n = 172)
Age (y $\pm$ SD)	50.6 ( $\pm$ 8.6)	51.3 ( $\pm$ 8.9)
BMI (kg/m <sup>2</sup> $\pm$ SD)	26.1 ( $\pm$ 3.1)	26.0 ( $\pm$ 2.6)
Prior radiotherapy, n (%)	17 (40.5%)	126 (73.3%)
Prior chemotherapy, n (%)	26 (61.9%)	132 (76.7%)

**Table 3. Intraoperative Data on Anesthesia and Fluid Management**

Intraoperative Procedures	No. Patients (%)	
	LFM Protocol (n = 42)	MFM Protocol (n = 172)
Inhalation agent		
Isoflurane	16 (38.1)	38 (22.1)
Sevoflurane	25 (59.5)	133 (77.3)
Other	1 (2.4)	1 (0.6)
Propofol		
Not used	27 (64.3)	5 (2.9)
Throughout the procedure	1 (2.4)	45 (26.2)
Final 2 h	11 (26.2)	100 (58.1)
Final 3 h		16 (7.5)
Final 4 h		5 (2.3)
Single bolus	1 (2.4)	1 (0.6)
Multiple boluses	2 (3.2)	
Vasopressor agent		
Not used	41 (97.6)	13 (7.6)
Norepinephrine		158 (91.9)
Dopamine	1 (2.4)	1 (0.6)
Colloid type		
Not used	14 (33.3)	164 (95.3)
Macrodex	21 (50.0)	8 (4.7)
Voluven	2 (4.8)	
Macrodex + Voluven	4 (9.5)	
Other	1 (2.4)	
Hypotensive episodes		
None	18 (42.8)	154 (89.5)
One	11 (26.2)	10 (5.8)
Several	13 (31.0)	8 (4.7)

compared with  $29.6 \pm 10.6$  ml/kg for the MFM cohort ( $P < 0.05$ ).

In the LFM cohort, 28 patients (66.6%) received colloids (Macrodex, Meda AS, Asker, Norway or Voluven, Fresenius Kabi Deutschland GmbH, Bad Homburg, Germany) compared with eight patients (4.7%) in the MFM cohort. While 159 patients (92.5%) in the MFM cohort received vasopressors, only one (2.4%) did so in the LFM cohort ( $P < 0.05$ ). Multiple hypotensive episodes occurred in 13 patients (31%) of the LFM cohort compared with eight patients (4.7%) in the MFM cohort ( $P < 0.05$ ).

Preoperative hemoglobin and hematocrit levels did not differ significantly between cohorts. The average intraoperative blood loss was higher in the LFM cohort than in the MFM cohort, at  $443.8 \pm 250.2$  ml and  $201 \text{ ml} \pm 124.1 \text{ ml}$ , respectively ( $P < 0.05$ ). Eight patients, of which five (11.9%) were in the LFM cohort, needed blood transfusion, all postoperatively, mainly because of dizziness during mobilization.

### Surgical Parameters

Data related to surgical procedures are presented in Table 5. The deep inferior epigastric perforator flap (DIEP) was the most frequently used flap in both cohorts. Contrarily, pedicled transverse rectus abdominis musculocutaneous flaps and free superficial inferior epigastric artery flaps comprised over 40% of the flaps in the LFM cohort. Procedure time or flap weight did not differ significantly. Venous superdrainage was more common in the MFM cohort (73.8%) compared with the LFM cohort (35.7%) ( $P < 0.05$ ).

**Table 4. Intraoperative Fluid Measures and Data on Blood Parameters**

Measures	LFM Protocol (n = 42)	MFM Protocol (n = 172)
Total fluid volume (ml $\pm$ SD)	4618.3 ( $\pm$ 1857.8)	3141.5 ( $\pm$ 768.3)
Total fluid per weight (ml/kg $\pm$ SD)	64.3 ( $\pm$ 24.3)	43.8 ( $\pm$ 10.5)
Fluid/weight/procedure time (ml/kg/h $\pm$ SD)	11.0 ( $\pm$ 5.7)	6.8 ( $\pm$ 1.7)
Colloid in treated population (ml $\pm$ SD)	741.1 ( $\pm$ 391.6)	443.8 ( $\pm$ 140.0)
Colloid/weight in treated population (ml/kg $\pm$ SD)	10.2 ( $\pm$ 5.3)	6.5 ( $\pm$ 2.0)
Total urine output (UO) (ml $\pm$ SD)	769.3 ( $\pm$ 516.6)	1019.0 ( $\pm$ 662.0)
Total UO per weight (ml/kg $\pm$ SD)	10.5 ( $\pm$ 6.5)	14.3 ( $\pm$ 9.3)
Fluid balance (ml/kg $\pm$ SD)	3849.0 ( $\pm$ 1608.7)	2122.6 ( $\pm$ 791.4)
Fluid balance per weight (ml/kg $\pm$ SD)	53.8 ( $\pm$ 22.0)	29.6 ( $\pm$ 10.6)
Intraoperative blood loss (ml $\pm$ SD)	443.8 ( $\pm$ 250.2)	201.0 ( $\pm$ 124.1)
Preoperative hemoglobin (gr/dl $\pm$ SD)*	13.1 ( $\pm$ 0.9)	13.5 ( $\pm$ 0.9)
Preoperative hematocrit (% $\pm$ SD)†	37.2 ( $\pm$ 3.5)	40.6 ( $\pm$ 2.9)
Postoperative hemoglobin (gr/dl $\pm$ SD)‡	9.9 ( $\pm$ 1.2)	11.4 ( $\pm$ 1.1)
Postoperative hematocrit (% $\pm$ SD)§	28.7 ( $\pm$ 3.7)	34.4 ( $\pm$ 3.3)
$\Delta$ Hemoglobin (gr/dl $\pm$ SD)	-3.2 ( $\pm$ 1.2)	-2.1 ( $\pm$ 1.0)
$\Delta$ Hematocrit (% $\pm$ SD)	-8.1 ( $\pm$ 4.3)	-6.1 ( $\pm$ 2.8)

\*Missing data from 2/172 (1%) patients in MFM cohort.

†Missing data from 16/42 (38%) in LFM cohort and 20/172 (11%) in MFM cohort.

‡Missing data from 7/42 (18%) patients in LFM cohort and 4/172/151 (2%) in MFM cohort.

§Missing data from 22/42 (52%) patients in LFM cohort and 10/172 (6%) in MFM cohort.

**Table 5. Intraoperative Data on the Surgical Procedures**

	LFM Protocol (n = 42)	MFM Protocol (n = 172)
Procedure time (min $\pm$ SD)	372.1 ( $\pm$ 106.0)	398.2 ( $\pm$ 82.3)
Flap weight (g $\pm$ SD)	717.7 ( $\pm$ 220.7)	686.1 ( $\pm$ 180.4)
Flap type, n (%)		
DIEP	23 (54.8 %)	138 (80.2 %)
MS-1 TRAM	2 (4.8 %)	25 (14.5 %)
Pedicled TRAM	13 (31.0 %)	4 (2.3 %)
SIEA	4 (9.5 %)	5 (2.9 %)
Venous drainage, n (%)		
DIEV to IMV	27 (64.3 %)	45 (26.2 %)
Double DIEV to IMV	1 (2.4 %)	30 (17.4 %)
SIEV to CV	14 (33.3 %)	56 (32.6 %)
Double DIEV to IMV + SIEV to CV		18 (10.5 %)
SIEV to IMV		13 (7.6 %)
Other		10 (5.8 %)

CV: cephalic vein; DIEV: deep inferior epigastric vein; IMV: internal mammary vein; MS-TRAM: muscle sparing transverse rectus abdominis myocutaneous flap; SIEA: superficial inferior epigastric artery perforator flap; SIEV: superficial inferior epigastric vein.

**Outcome**

Outcome data are presented in Table 6. Intraoperative complications were more frequent in the LFM cohort compared with those in the MFM cohort, at 28.6% and 14.5%, respectively ( $P < 0.05$ ). Intraoperative blood loss (>500 ml) was the most frequent complication in the LFM cohort and vascular pedicle problems in the MFM cohort.

Postoperatively, surgical and medical complications were more frequent in the LFM cohort. The higher incidence of surgical complications, observed in 27 patients (42.9%), when compared with in 33 patients (21.9%) in the MFM cohort, was mainly related to partial and total flap failures ( $P < 0.05$ ). Postoperative flap complications due to vascular insufficiency occurred in 38 patients. Emergent exploration was performed in 12 flaps, of which three were salvaged. Other postoperative surgical complications were scarce, apart from a significantly higher occurrence of postoperative hematoma in the MFM cohort [12 patients (7%)], mainly related to the abdominal donor site. Medical complications, mostly respiratory distress, were reported in six patients (14.3%) in the LFM cohort and four patients (2.3%) in the MFM cohort ( $P < 0.05$ ). Mean length of stay (LOS) was significantly longer in the LFM cohort at 12.7 ( $\pm 6.5$ ) days compared with 10.5 ( $\pm 2.7$ ) days for the MFM cohort ( $P < 0.05$ ).

Logistic regression analysis showed a statistically significant association between the applied fluid management protocol and intraoperative and postoperative complications (Table 7). The MFM protocol was more beneficial, resulting in reduced odds for complications in the range of 57%–85% compared with the LFM protocol. Propofol was not independently associated with outcome. Likewise, prior radiotherapy, type of inhalation agent, or venous superdrainage did not have a statistically significant impact on outcome. Post-hoc analysis within the LFM

**Table 7. Regression Analysis of Outcome per Fluid Management Protocol**

Complications	No. Patients (%)		P	Odds Ratio (95% CI)
	LFM Protocol (n = 42)	MFM Protocol (n = 172)		
Intraoperative	12 (28.6)	25 (14.6)	0.034	0.425 (0.192–0.939)
Postoperative surgical	22 (52.3)	33 (22.1)	0.000	0.284 (0.140–0.573)
Postoperative medical	6 (14.3)	4 (2.3)	0.004	0.143 (0.038–0.532)

cohort found no significant association between flap type and the incidence of surgical complications.

Postoperative complications reduced considerably after 2003, associated with a concurrent reduction of intraoperative fluid resuscitation and end-surgery fluid accumulation. The complication rate was further reduced with full implementation of the MFM protocol in 2005 (Fig. 1).

**DISCUSSION**

The MFM protocol resulted in fewer complications for unilateral autologous breast reconstructions compared with the LFM protocol. Plausible explanations are discussed.

**Fluid Resuscitation**

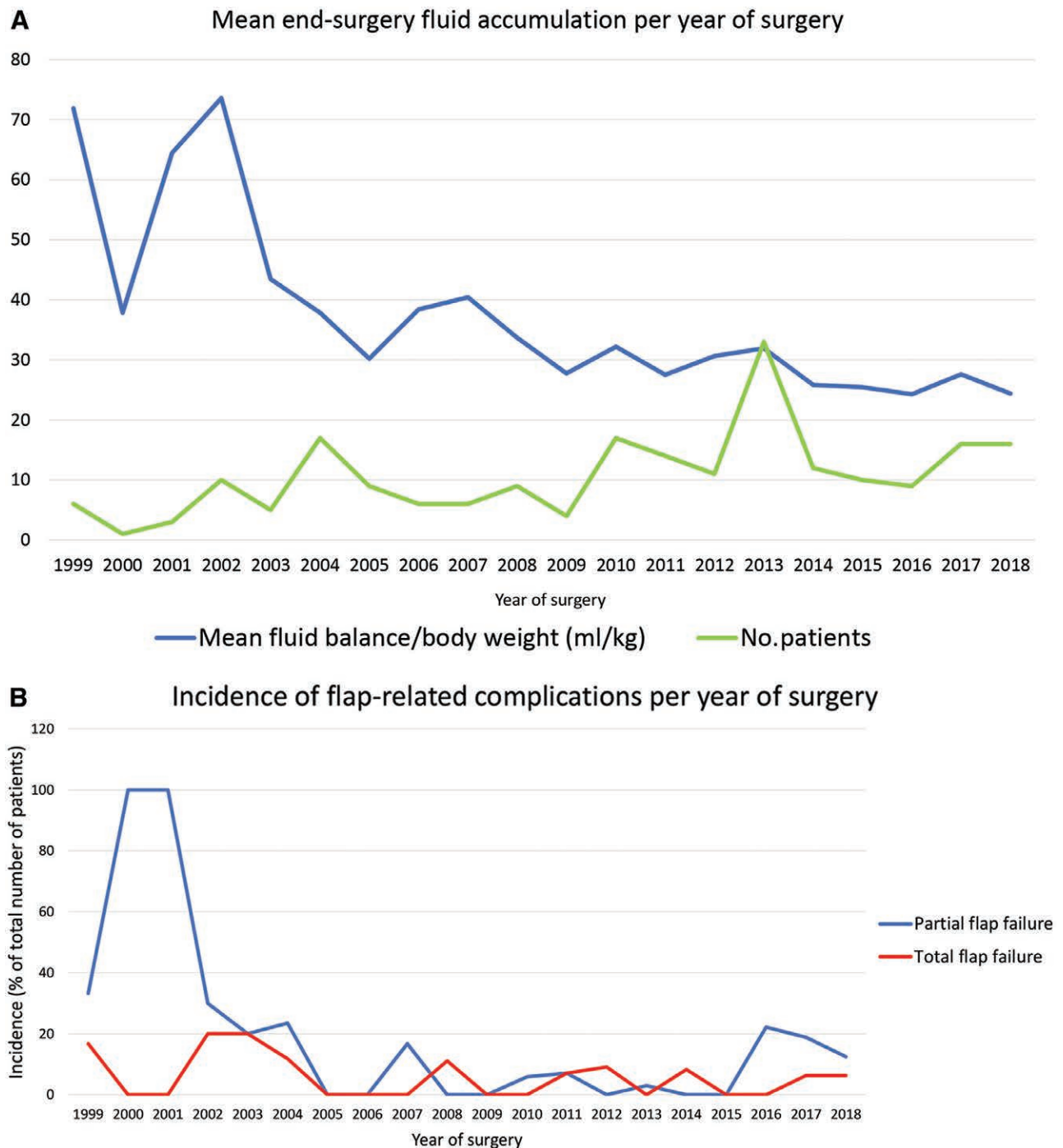
Insensible loss and fluid shifting have been the rationale for large volume resuscitation in the past. Recent studies have found these estimations incorrect.<sup>12,13</sup> Intraoperative fluid overload results in tissue edema and an increased risk of postoperative complications and prolonged recovery.<sup>13</sup> Flap-related complications are more common when using a LFM.<sup>7,8,14,15</sup> Intraoperative crystalloid volumes exceeding 7L, or 130 ml/kg/day have been associated with major medical and surgical complications.<sup>7</sup> The ideal intraoperative crystalloid infusion rate is reported to be in the range of 3.5–6 ml/kg/h.<sup>8</sup>

The mean intravenous fluid volume in the LFM cohort was 11 ml/kg/h, versus 6.8 ml/kg/h in the MFM cohort (Table 4). More noteworthy, as the intraoperative urine output was lower in the LFM cohort, the net fluid accumulation at the end of surgery was significantly larger in the LFM cohort. We think that fluid accumulation is more important that the fluid infusion rate, as the end-surgery interstitial edema should be directly correlated to the actual fluid uptake. Karamanos et al observed a positive impact on outcome with strict fluid management during free flap breast reconstructions.<sup>15</sup> The fluid accumulation in their restricted cohort (4.8 ml/kg/hr) mirrors the findings in our MFM cohort (4.6 ml/kg/h). Furthermore, in a goal-directed fluid therapy (GDFT) study on pedicled and free flap breast reconstructions, Polanco et al registered a net fluid accumulation of 317 ml/h for patients following an enhanced recovery after surgery (ERAS) protocol.<sup>16</sup> This was almost similar to the end-surgery fluid balance in our MFM cohort (325 ml/h). Extracellular colloid leakage may contribute to such fluid entrapment and prolonged edema.<sup>17,18</sup> The more frequent colloid use

**Table 6. Observed Adverse Events and LOS**

	LFM Protocol (n = 42)	MFM Protocol (n = 172)
Intraoperative complications, n (%)		
None	30 (71.4%)	147 (85.5%)
Bleeding (>500 ml)	8 (19.0%)	2 (1.2%)
Inadequate flow in recipient artery	3 (7.1%)	7 (4.1%)
Arterial thrombosis		11 (6.4%)
Venous congestion	1 (2.4%)	1 (0.6%)
Other		4 (2.3%)
Postoperative surgical complications, n (%)		
None	20 (47.6%)	134 (77.9%)
Bleeding		12 (7.0%)
Infection	1 (2.4%)	5 (2.9%)
Wound rupture		4 (2.3%)
Partial necrosis	14 (33.3%)	11 (6.4%)
Total flap loss	6 (14.3%)	6 (3.5%)
Hernia	1 (2.4%)	
Postoperative medical complications, n (%)		
None	36 (85.7%)	168 (97.7%)
Pulmonary embolism	1 (2.4%)	
Respiratory distress	3 (7.1%)	3 (1.7%)
Urinary tract infection	1 (2.4%)	
Other	1 (2.4%)	1 (0.6%)
Length of stay, d ( $\pm$ SD)	12.7 ( $\pm 6.5$ )	10.5 ( $\pm 2.7$ )





**Fig. 1.** Fluid accumulation and flap complications. A, Yearly distribution of mean end-surgery fluid balance in the patient population during the study period. A notable reduction is seen after 2002. B, Distribution of the incidence of flap-related complications per year during the study period. The incidence of partial flap failure (blue line) is generally higher than the incidence of total flap failure (red line). Flap-related complications were remarkably fewer after 2002/2003.

in the LFM cohort could be a plausible explanation for the larger fluid accumulation compared with the MFM cohort, although statistical analysis did not find an independent association between the use of colloids and outcome in the present study. Post-hoc analysis showed that intra- or postoperative bleeding (>500 ml) was significantly more common among patients who had received colloids,

which are known to alter hemostasis.<sup>19</sup> No other adverse events associated with colloids were observed.<sup>5,20</sup> Others reported that colloids are safe to use in flap surgery.<sup>14,21,22</sup>

Fluid resuscitation using small volumes may be insufficient to correct hypotension, resulting in an increased risk for complications, especially in patients with preoperative comorbidities.<sup>13,23</sup> An individualized GDFT can therefore

be a beneficial fluid management strategy in autologous breast reconstructions.<sup>16</sup>

### Ischemia-reperfusion Injury

IRI in free flap surgery can be a significant risk factor for adverse events.<sup>6</sup> Prolonged duration of ischemia is associated with increasing risk of flap loss.<sup>24</sup> Propofol inhibits platelet aggregation, induces vasodilation, and protects against adverse effects of free radicals after flap reperfusion.<sup>25,26</sup> Propofol was an essential part of the MFM protocol and might have had a beneficial impact on the outcome, although not detectable on statistical analysis.

### Anesthesia

Isflurane and sevoflurane preserve a high cardiac output and adequate microcirculatory flow.<sup>27</sup> Sevoflurane is particularly beneficial in flap surgery, as it reduces capillary leakage of plasma into the interstitial space and protects against IRI, thereby limiting tissue edema.<sup>28,29</sup> The combination of sevoflurane and propofol was essential in the MFM protocol. Independent association with outcome was not observed for either drug, but we believe that a synergistic effect of these contributed to the beneficial outcomes in the MFM cohort.

### Vasoactive Agents

At the time of introduction of our MFM protocol in 2005, few reports supported the use of vasoactive drugs in free flap surgery. Prior animal studies presented contradictory results regarding the impact of vasoconstrictive agents on flap perfusion, resulting in a general notion that vasopressors could increase the risk of peripheral vasospasm, thrombosis, and flap failure.<sup>9</sup> Yet, some studies reported findings of increased flap perfusion when utilizing inotropic drugs.<sup>30,31</sup> We included norepinephrine in the MFM cohort to maintain adequate blood pressure, the benefits of which have later been advocated by Eley et al in a study comparing the effect of several vasoactive drugs on flap perfusion.<sup>32</sup>

The short half-life of most vasopressors facilitates a more precise intraoperative control of the blood pressure, which in turn will contribute to reduce the risk of poor outcome.<sup>2</sup> The higher urine output in the MFM cohort can partially be explained by the effect of norepinephrine, promoting increased kidney perfusion. Norepinephrine also mitigated intravenous fluid resuscitation, as adequate blood pressure could be upheld without the need for additional intravenous fluid. The safety of vasoactive agents in reconstructive microsurgery observed in this study falls in line with the findings of several recent publications.<sup>9,33,34</sup>

### Postoperative Hemodilution

The impact of reduced oxygen-carrying capacity resulting from hemodilution or anemia has been debated. Velanovich et al and Mlodinow et al found no association between low hematocrit and flap failure.<sup>35,36</sup> Others have demonstrated a negative effect of a hematocrit level at 24%.<sup>8,37</sup> Sigurdsson et al recommended a hematocrit level at 30%–35% to achieve optimal viscosity and oxygen-carrying capacity.<sup>38</sup> In our study, postoperative hematocrit

levels were at 31.1% in the LFM cohort and 34.5% in the MFM cohort. The difference between pre- and postoperative hematocrit levels was larger in the LFM cohort, which can be explained by hemodilution due to higher volumes of crystalloid infusion and more frequent use of colloids.

### Surgical Factors

Pediced flaps were more frequent in the LFM cohort. Pedicled or free TRAM flaps were chosen when perforators were insufficient to allow for DIEP breast reconstruction. Although some reports have found free flaps to be an independent risk for ischemic flap complications, others have found no such association.<sup>39–41</sup> Addressing surgical site complications specifically, Masoomi et al found no correlation with different flap types (free or pedicled).<sup>42</sup> No association between flap type and complications was observed on intracohort analysis among patients following the LFM protocol. However, the more frequent intraoperative bleeding in the LFM cohort might have been related to the more traumatic dissection in pedicled transverse rectus abdominis musculocutaneous flaps when compared with the delicate dissection in DIEP flaps.

Insufficient venous drainage is the most frequent cause of flap complications.<sup>43,44</sup> Venous superdrainage was more frequent in the MFM cohort compared with the LFM cohort, but venous superdrainage per se did not have an independent impact on the postoperative outcome of flap complications. In a recent meta-analysis, Lee et al did not find sufficient evidence to advocate such procedures in autologous breast reconstruction.<sup>45</sup> Thus, one could postulate that an overzealous use of venous super-drainage was performed in the present study.

### Radiation Therapy

Although prior radiation therapy in breast reconstructions has been associated with an increased risk of complications, the present study found no significant impact of prior radiotherapy on outcome.<sup>46</sup>

### Length of Stay

Several reports from different surgical disciplines state that shorter length of stay (LOS) can be achieved with multimodal analgesia, patients of lower American Society of Anesthesiologists class, and implementation of ERAS protocols. Correspondingly, long-lasting surgery and anesthesia as well as excessive fluid administration are known to lengthen hospitalization.<sup>47,48</sup> A recent publication assessing ERAS in free flap breast reconstructions demonstrated a significantly shorter LOS, with less opioid and antiemetic use and with no increase in the rate of major complications.<sup>49</sup> Polanco et al in their study on ERAS with goal-directed fluid therapy also noted a decrease in LOS after the implementation of ERAS, but stated that the preoperative counseling on shorter hospitalization itself might have influenced patients' expectations in terms of LOS.<sup>16</sup> Although we did not specifically implement preoperative counseling in the MFM protocol, we observed a reduced LOS in this patient cohort. Patients in the MFM cohort were mobilized earlier, whereas patients in the LFM cohort were more frequently hindered by dizziness

and peripheral edema. We anticipate that the restrictive fluid management was the main factor influencing LOS. The geographical nature of our catchment area, with many patients traveling long distances to our hospital, may have mitigated the potential difference in LOS between cohorts.

### Limitations

The retrospective approach of this study is an obvious limitation. The small number of patients, especially in the LFM cohort, limits the validity of our findings. The follow-up period of our patients was short. The multimodal nature of our modifications to the fluid management protocol did not allow assessment of the independent impact of certain variables, such as colloids or norepinephrine. We still postulate that the synergistic effect of these modifications contributed to the improved outcomes in the MFM cohort.

An obvious source of bias is the learning curve related to complex procedures. This relates to both technical details of flap surgery and to a general know-how in the surgical and anesthetic team. The higher complication rate in the LFM cohort could be partially attributed to inexperience. Several studies report a higher incidence of adverse events during the first 30 cases.<sup>50,51</sup> In contrast, Grinsell et al reported that the complication rate did not differ between early and late cases and attributed this to a more widespread knowledge on flap surgery during recent years.<sup>52</sup> Even if no significant difference in procedure time between cohorts was observed in the present study, the advantage of skilled staff without doubt supports successful outcome and might therefore have resulted in unjust acclaim for the MFM protocol. Yet, the rather “dramatic” improvement in complication rates with the introduction of the MFM protocol seems more likely related to the modifications in fluid management than to the expected improved prognosis plainly due to increased team-competence.

### CONCLUSION

Reduced intraoperative fluid resuscitation combined with optimized blood pressure control by using norepinephrine and propofol can result in fewer complications in unilateral abdominal-flap breast reconstruction.

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