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Impact of Intraoperative Hypothermia on Microsurgical Free Flap Reconstructions

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Abstract

Background Patients requiring microsurgical defect reconstruction are highly susceptible to intraoperative hypothermia, given oftentimes long operative times and exposure of large skin surface areas. While the impact of hypothermia has been extensively studied across various surgical fields, its role in the setting of microsurgical free flap reconstruction remains elusive. This study evaluates the effects of hypothermia on outcomes of free flap reconstructions.

Methods Within 7 years, 602 patients underwent 668 microvascular free flap reconstructions. The cases were divided into two groups regarding the minimal core body temperature during free flap surgery: hypothermia (HT; < 36.0°C) versus normothermia (NT; ≥ 36.0°C). The data were retrospectively screened for patients' demographics, perioperative details, flap survival, surgical complications, and outcomes.

Results Our data revealed no significant difference with regard to the rate of major and minor surgical complications, or the rate of revision surgery between both groups ($p > 0.05$). However, patients in the HT group showed significantly higher rates of total flap loss (6.6% [HT] vs. 3.0% [NT], $p < 0.05$) and arterial thrombosis (4.6% [HT] vs. 1.9% [NT], $p < 0.05$). This translated into a significantly longer hospitalization of patients with reduced core body temperature (HT: mean 16.8 days vs. NT: mean 15.1 days; $p < 0.05$).

Conclusion Hypothermia increases the risk for arterial thrombosis and total flap loss. While free flap transfer is feasible also in hypothermic patients, surgeons' awareness of core body temperature should increase. Taken together, we suggest that the mean intraoperative minimum temperature should range between 36 and 36.5°C during free flap surgery as a pragmatic guideline.

Keywords
- hypothermia
- free flap reconstruction
- risk constellation
- temperature
- outcome

Microsurgical reconstructions have become routine procedures in plastic surgery and are performed for a wide range of defects all over the body.[1–3] Yet, vascular compromise continues to account for revision rates between 5 and 25%.[4,5] Several patient-related factors, such as smoking, diabetes, old age, and preoperative American Society of Anesthesiologists (ASA) scores, have been discussed controversially with regard to the safety and efficacy of microsurgical reconstructions.[6–9] However, our study group previously demonstrated that these factors pose no contraindication for free flap reconstructions,

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showing no significant impact on overall free flap outcomes.[10–12] To further reduce complication rates, potential additional risk factors need to be identified and their impact on free flap outcome evaluated.

Recently, the role of intraoperative hypothermia has gained attention.[13–16] Free-flap reconstructions are regularly performed in two operating teams.[17] This exposes large skin surface areas, which increases patients' susceptibility to hypothermia.[15,18] In general, hypothermia causes peripheral vasoconstriction, an increase in blood viscosity and a reduced blood flow, which can ultimately lead to increased thrombogenic potential.[14,19–21] Conversely, therapeutic hypothermia has been shown to reduce hypoxemia and ischemia in a wide range of different settings, such as acute myocardial infarction[22,23] or organ preservation, prior to transplantation.[24]

In the context of free-tissue transfer, it remains unclear whether hypothermia results in decreased perfusion, vasospasm, and thrombosis, or exerts protective effects associated with higher rates of flap patency and survival.[13,14,16,20,25] Current studies have suggested that mild hypothermia may improve flap outcome; however, they are based on limited case numbers or animal models.[14–16]

Given the controversies, we analyzed our single surgical center experiences to evaluate the incidence, cause and effects of hypothermia on outcomes of free flap reconstructions.

Patients and Methods

Over a period of 7 years, 668 free flap surgeries were performed after trauma, infection, or malignancies. Continuous core body temperature (°C) was measured and documented in all cases by the use of a urinary bladder monitoring system. Hypothermia is defined variably in the literature. In our study, the cut-off was chosen based on standard anesthesiologic guidelines. These determine a core temperature of < 36°C to be hypothermic.[26–28] Normothermia (NT) was defined as a consistent intraoperative core body temperature of equal or higher than 36.0°C. Hypothermia (HT) was defined as an intraoperative body temperature of less than 36.0°C in any given measurement during the continuous monitoring process. In all patients, the temperature at the beginning of the surgery and the maximum decrease was documented. During surgery, all patients were placed on heating mats and wherever possible, the patients were covered by one-way blankets, as well as sterile surgery coverages.

To create a matched-cohort analysis of the effect of intraoperative hypothermia on free flap reconstructions, the medical files and patient data were retrospectively screened for patients' demographics, perioperative details, flap survival, surgical, and medical complications. There were no distinct exclusion criteria. However, a complete preoperative dataset for every patient to be included was mandatory.

Taking into account, the possible influence of medical conditions on postoperative outcomes, the preoperative medical status of each patient was assessed and classified according to the ASA score of physical status. The anesthesiologist in charge determined this score for every patient. Patients having preoperative scores of ASA I and II were defined as "low-risk" patients, and those of ASA III and IV as "high-risk" patients.

Surgical complications were accounted for and defined as major (total flap loss, arterial or venous thrombosis, hematoma, and partial flap loss of $> 10\%$) or minor complications (wound dehiscence, skin graft failure, wound infection, and partial flap loss of $<10\%$). The microsurgical reconstructions were then divided into two groups regarding the minimal core body temperature measured during free flap surgery: HT (< 36.0°C) versus NT (≥ 36.0°C).

Statistical Analysis

Chi-squared analysis with Fisher's exact tests was used to determine the effect of temperature on complication rates and free flap outcome. The data showed a normal distribution. An unpaired *t*-test was also employed. Significance was defined for values of $p < 0.05$.

Results

The HT group included 271 patients who received 304 free flaps, the NT group included 331 patients who received 364 free flaps. The mean age of both groups was comparable ($p > 0.05$). Gender distribution showed a significantly higher percentage of male patients in the NT group (male: 63.4%; female: 36.6%) compared with the HT group (male: 46.1%; female: 53.9%; $p < 0.05$). Mean minimal temperature was 35.4 (0.41)°C in the HT group and 36.4 (0.31)°C in the NT group ($p = 0.000$). Regarding the preoperative evaluation, patients in the NT group showed a significantly higher prevalence of hypertension compared with the HT group (40.7 vs. 25.5%; $p < 0.05$), as well as a significantly higher prevalence of peripheral artery disease (PAD; 10.5 vs. 5.9%; $p < 0.05$) and diabetes mellitus (DM; 22.1 vs. 13.7%; $p < 0.05$). Therefore, the mean ASA score (HT: 2.2, standard deviation [SD] = 0.72 vs. NT: 2.4, SD = 0.76) was significantly higher in the NT compared with the HT group. In contrast, the prevalence of smoking was significantly higher in the HT group (HT: 28.1 vs. NT: 20.9%; $p < 0.05$). Analysis of the prevalence of obesity defined as a body mass index (BMI) of equal or higher than 30 (25.5 vs. 24.5%; $p = 0.061$) showed no significant difference between both groups. Patient demographics are summarized in ►**Table 1**.

Several types of free flaps were used for defect reconstruction (►**Table 2**). Significant differences between both groups with regard to flap type were found for DIEP (HT: 16.1% vs. NT: 7.4%), gracilis muscle (HT: 20.4% vs. NT: 32.4%), and latissimus dorsi muscle flap reconstructions (HT: 8.9% vs. NT: 3.6%; $p < 0.05$). Overall, reconstructions in the HT group showed a significantly higher number of fasciocutaneous flaps, whereas the NT group contained significantly more muscle free flap reconstructions ($p < 0.05$).

Regarding the recipient sites, the HT group underwent significantly more microsurgical head and neck procedures, as well as reconstructions of trunk defects ($p < 0.05$). However, in the NT group significantly more lower extremity reconstructions were performed ($p < 0.05$). The etiology for free flap reconstructions also revealed significant differences between both groups ($p < 0.05$; ►**Table 2**)

Table 1 Patient demographics according to core body temperature (°C) during free flap surgery, as measured by a urinary bladder monitoring system

Characteristics	HT (< 36°C)	NT (≥ 36°C)	*p*-Value
Number of patients (*n*)	**271 (%)**	**344 (%)**	
Male	125 (46.1)	218 (63.4)	0.002
Female	146 (53.9)	126 (36.6)	
Mean age (y)	51.4	52.5	0.434
Range of age (y)	18–91	18–80	
SD (y)	18.1	16.2	
Comorbidities (n)			
Hypertension	69 (25.5)	140 (40.7)	0.000
PAD	16 (5.9)	36 (10.5)	0.044
Diabetes mellitus	37 (13.7)	76 (22.1)	0.007
Mean BMI (SD)	24.1 (9.62)	23.9 (5.74)	0.762
Range BMI	15.6–42.2	16.1–40.9	
Mean ASA (SD)	2.2 (0.72)	2.4 (0.76)	0.001
Smoking status (*n*)			
Nonsmoker	195 (71.9)	272 (79.1)	0.040
Smoker	76 (28.1)	72 (20.9)	
Temperature (°C)			
Mean min. (SD)	35.4 (0.41)	36.4 (0.31)	0.000
Range min.	33.7–35.9	36.0–37.3	
Mean max. (SD)	36.4 (0.52)	37.2 (0.48)	0.000
Range max.	34.6–38.0	36.1–39.0	
Mean change (SD)	1.0 (0.52)	0.76 (0.41)	0.000
Range change	0.1–3.3	0–2.8	

Abbreviations: ASA, American Society of Anesthesiologists Classification of physical status; BMI, body mass index; HT, hypothermia; max., maximum; min., minimum; NT, normothermia; PAD, peripheral arterial disease; SD, standard deviation.

Analysis of flaps dimensions (cm^2), mean operative times (min), as well as mean ischemic times (min), did not show any significant difference between both groups ($p > 0.05$; ►**Table 2**).

Overall, there was no significant difference between the two groups of patients regarding the rate of major and minor surgical complications, as well as of partial flap loss >10% during our 3-month follow-up period ($p > 0.05$). Additionally, our data showed no significant difference with regard to the rate of surgical revision surgery ($p > 0.05$). However, the total percentage of total flap losses of 6.6% (HT) versus 3.0% (NT) showed a significant difference between the two groups ($p < 0.05$).

Analysis of reasons for revision surgery revealed significantly more arterial thrombosis in the HT group ($p < 0.05$); whereas both groups had similar total percentages of venous thrombosis and bleeding complications ($p > 0.05$; ►**Table 3**)

Statistical analysis of hospital length of stay revealed significant differences when comparing both groups (HT: mean = 16.8 days, range: 5–68 days, SD = 9.9 days vs. NT: mean = 15.1 days, range: 4–42 days, SD = 7.8 days; $p < 0.05$).

Table 2 Flap characteristics according to core body temperature (°C) during free flap surgery, as measured by a urinary bladder monitoring system

Characteristics	HT (< 36°C)	NT (≥ 36°C)	*p*-Value
Flap type (*n*)	(%)	(%)	
ALT	84 (27.6)	117 (32.1)	0.206
Groin	27 (8.9)	26 (7.1)	0.408
DIEP	49 (16.1)	27 (7.4)	0.000
RFA	9 (3.0)	8 (2.2)	0.533
Parascapular	8 (2.6)	10 (2.7)	0.927
ELAF	5 (1.6)	12 (3.3)	0.177
Gracilis	62 (20.4)	118 (32.4)	0.000
LDM	27 (8.9)	13 (3.6)	0.004
Others	33 (10.9)	33 (9.1)	0.440
Recipient sites (*n*)			
Upper extremity	43 (14.1)	62 (17.0)	0.307
Lower extremity	128 (42.1)	211 (58.0)	0.000
Head and neck	61 (20.1)	49 (13.5)	0.022
Trunk	72 (23.7)	42 (11.5)	0.000
Etiology for free flap			
Trauma	164 (53.9)	224 (61.5)	0.048
Infection	34 (11.2)	71 (19.5)	0.003
Malignancies	106 (34,9)	69 (19.0)	0.000
Flap dimension			
Size (cm^2)	217.4	198.9	0.170
Range (cm^2)	25–1400	24–1535	
SD (cm^2)	161.6	186.4	
Mean operative time (min)	359.2	359.9	0.942
Range (min)	65–720	117–900	
SD (min)	112.7	133.8	
Mean ischemic time (min)	56.1	59.7	0.109
Range (min)	23–180	15–190	
SD (min)	27.6	30.3	
Total flaps (*n*)	304	364	

Abbreviations: ALT, anterolateral thigh; DIEP, deep inferior epigastric perforator; ELAF, extended lateral arm flap; HT, hypothermia; LDM, latissimus dorsi; NT, normothermia; RFA, radial forearm; SD, standard deviation.

Further investigation of intraoperative core body temperature differences between extremity and trunk reconstructions revealed no major temperature differences with regard to the location of the defect (►**Table 4**; $p > 0.05$).

Discussion

Microsurgical reconstruction has become the standard of care for the reconstruction of complex defects. Overall complications of these complex operations have decreased

Table 3 Postoperative complications according to core body temperature (°C) during free flap surgery, as measured by a urinary bladder monitoring system

Complication	HT (< 36°C) (%)	NT (≥ 36°C) (%)	*p*-Value
Major	84 (27.6)	95 (26.1)	0.656
Total flap loss	20 (6.6)	11 (3.0)	0.029
Partial flap loss >10%	17 (5.6)	26 (7.1)	0.416
Revision surgery	47 (15.5)	58 (15.9)	0.881
Arterial thrombosis	14 (4.6)	7 (1.9)	0.048
Venous thrombosis	20 (6.6)	30 (8.2)	0.416
Hematoma	13 (4.3)	21 (5.8)	0.382
Minor[a]	36 (11.8)	37 (10.2)	0.489
Mean Hospitalization (d)	16.8	15.1	0.015
Range (d)	5–68	4–42	
SD (d)	9.9	7.8	
Total flaps (*n*)	304	364	

Abbreviation: SD, standard deviation.
[a]Wound dehiscence, skin graft failure, wound infection, and partial flap loss < 10%.

Table 4 Comparison of patients' core body temperature (°C) during free flap surgery at extremities or trunk, as measured by a urinary bladder monitoring system

Characteristics	Extremity	Trunk	*p*-Value
HT (< 36°C) (*n*)	171	72	
Mean min. (SD)	35.4 (0.39)	35.3 (0.41)	0.079
Range min.	34.0–35.9	34.1–35.9	
Mean max. (SD)	36.5 (0.55)	36.4 (0.51)	0.174
Range max.	34.6–39.2	35.2–37.7	
Mean change (SD)	1.0 (0.53)	1.0 (0.58)	1.000
Range change	0.2–3.3	0.1–4	
NT (≥36°C) (*n*)	273	42	
Mean min. (SD)	36.4 (0.36)	36.3 (0.30)	0.051
Range min.	36.0–37.3	36.0–37.0	
Mean max. (SD)	37.2 (0.43)	37.2 (0.38)	1.000
Range max.	36.3–39.0	36.4–37.8	
Mean change (SD)	0.74 (0.36)	0.66 (0.32)	0.139
Range change	0.2–1.5	0.2–1.5	

Abbreviations: HT, hypothermia; max., maximum; min., minimum; NT, normothermia; SD, standard deviation.

significantly, given a continuous improvement in microsurgical techniques and technology, efficient management of comorbidities, and progress in terms of anesthesia, as well as perioperative management.[29–32] Nonetheless, free flap transfers require high technical expertise and skill and continue to be relatively risky compared with other standard procedures. Complex defect reconstructions are often associated with long operative time, broad tissue dissection, compromised tissue perfusion and ischemia.[29,33–35] Consequently, the impact of several potential risk factors on outcomes of microvascular free tissue transfer have been elucidated.[10–12]

In the presented study, aim was to further evaluate the controversially debated role of intraoperative hypothermia on free flap outcomes.

We observed no significant relationship between location of the defect and patients' intraoperative core body temperature. Analysis of major complications revealed a significantly higher number of total flap losses in hypothermic patients (6.6% [HT] vs. 3.0% [NT]; $p < 0.05$). Evaluation of reasons for operative revision showed a significantly higher number of arterial thrombosis (4.6% [HT] vs. 1.9% [NT]; $p < 0.05$) in patients with reduced intraoperative core body temperature. These results stress the importance of perioperative temperature management. Motakef et al distributed an online survey consisting of questions regarding perioperative management for free tissue transfer and evaluated microsurgeons' approach to perioperative temperature control.[36] According to their data, intraoperative core temperature was assessed most commonly using an esophageal probe (69%), followed by the use of a Foley's catheter (35%). Unfortunately, their data provided no insight into the clinical pathways applied for patient temperature control or specific temperature goals. The study groups of Liu et al and Laitman et al previously set out to identify the optimal intraoperative body temperature during free flap surgery.[14,16] According to Liu et al, the optimal temperature is 36.2°C. In addition, they found that maximum intraoperative temperatures between 36.0 and 36.4°C show lower thrombosis rates compared with superwarmed patients ($p < 0.03$).[14] Laitman et al state that a mean intraoperative temperature of 36.5°C is protective against postoperative flap complications in head and neck reconstructions.[16] In line with this, our data show that temperature below 36°C is an independent risk factor for free flap outcome. Taken together, we suggest that the mean intraoperative minimum temperature should range between 36 and 36.5°C during free flap surgery as a pragmatic guideline.

According to the literature, hypothermia increases the rate of surgical site infections (SSI) in patients undergoing operative trauma procedures or colorectal surgery.[37–39] In contrast, for patients receiving free flap transfers, our data show no overall difference with regard to the rate of minor surgical complications between both groups, including wound dehiscence, skin graft failure, wound infection, and partial flap loss <10%. However, we found the length of hospitalization to be significantly higher in patients which had suffered reduced intraoperative core body temperature (HT: mean = 16.8 days vs. NT: mean = 15.1 days; $p < 0.05$). This might be attributed to the higher rates of total flap loss and the increase of arterial thrombosis in this patient group. This reinforces findings of studies across several surgical disciplines which describe an extended recovery time and prolonged hospitalization and associated costs for hypothermic patients.[39–41] Hart et al and Dimick et al estimated that an increase of hospitalization over 4 days, due to complications associated with hypothermia, results in an increased attributable cost of U.S. $8,000 to 25,000 per patient.[39,42] In times of rising economic pressure in health care, this further stresses the importance of maintaining intraoperative normothermia.

We found an unequal distribution of comorbidities and gender between both groups. The NT group included significantly more male patients. A higher number of patients in this group suffered from hypertension, PAD, and DM that translated into significantly higher ASA scores. On the other hand, we found a significantly larger number of females and smokers in the HT group. Several studies have evaluated risk factors for intraoperative hypothermia. These include old age, weight, systolic blood pressure, heart rate, and ASA score.[43,44] Patients with hypertension tend to become less hypothermic,[43,45] as indicated also by our data. Conversely, while studies have shown a high ASA physical status to be associated with an increased risk of hypothermia,[44] our data do not support this link. Literature on the relationship between gender and hypothermia is scarce and elusive.[46] Despite the apparent greater susceptibility of females for hypothermia in our study, further studies are necessary to strengthen this association. Importantly, in summary, the NT group included more "high-risk" patients, but showed significantly fewer complications (total flap loss and arterial thrombosis) compared with hypothermic patients. This finding further stresses the importance of maintaining intraoperative normothermia to improve flap outcomes.

While flap dimensions, mean operative and ischemic times were comparable between both groups, they differed with regard to flap types and recipient sites. In the HT group, more fasciocutaneous flaps were performed, while reconstructions in the NT group included significantly more muscle free flaps. Since the HT group showed significantly higher rates of total flap loss and arterial thrombosis, one could argue that this effect could be related to the higher amount of fasciocutaneous flaps performed in this group. However, Koepple et al recently compared fasciocutaneous and muscle-based free flap reconstructions of the upper extremity and found significantly higher rates of arterial thrombosis in muscle-based flaps.[47] Also, they found no significant difference with regard to total flap loss between both flap types.

The HT group underwent significantly more microsurgical reconstructions of the head and neck, while significantly more lower extremity reconstructions were performed in the NT group. To our knowledge, no studies have evaluated whether the risk of hypothermia is related to the free flap recipient site. Our data, however, allows no conclusion in this regard. An increased number of head and neck reconstructions could be attributed to the higher rate of smokers in the HT group, since smoking significantly increases the risk of cancer.[48] Patients in the NT group required significantly higher numbers of lower extremity reconstructions that probably results from significantly more defects after trauma in this group. In the future, prospective studies and pooling data of large microsurgical centers could help to further elucidate the impact of hypothermia on outcome of different free flap entities, also regarding the recipient sites.

Strengths and Limitations

A major strength of this study lies in the large sample size of 602 patients having received 668 free flap reconstructions at a single surgical center. Comparing 304 free flap reconstructions in hypothermic patients with 364 flaps in normothermic patients allowed us to draw significant conclusions regarding the impact of hypothermia on outcome and complications of free tissue transfers. Limiting factors of this study include its' retrospective character, as well as the inhomogeneity in both groups, with regard to preoperative medical status and gender distribution.

Conclusion

This study analyzed a large series of microsurgical free tissue transfers with regard to the impact of hypothermia on flap outcomes and complications. According to the presented data, hypothermia increases the risk for arterial thrombosis and total flap loss and should thus be avoided when performing microsurgical procedures. Taken together, we suggest that the mean intraoperative minimum temperature should range between 36 and 36.5°C during free flap surgery as a pragmatic guideline.

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Conflict of Interest
None declared.

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