Risk evaluation in cutaneous melanoma patients undergoing lymph node dissection: impact of POSSUM

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ABSTRACT

INTRODUCTION When lymphatic metastasis occurs, surgery is the primary treatment modality in melanoma patients. Depending on the tumour stage, patients receive a completion lymph node dissection (CLND) when a positive sentinel node is detected. Patients with clinically evident disease of the regional lymph nodes are recommended to undergo a therapeutic lymph node dissection (TLND). The aim of this study was to assess the morbidity of CLND and TLND and to evaluate the Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity (POSSUM) for preoperative risk adjustment of postoperative morbidity.

METHODS The hospital files of 143 patients who underwent CLND and TLND for malignant melanoma were analysed. The POSSUM score was used to predict morbidity rates after surgery for the total patient group as well as separated for CLND and TLND patients.

RESULTS The overall complication rate was 28.0% and the mortality rate was 0%. The morbidity rate predicted by POSSUM was 32.9%, the mortality 8.3%. Morbidity in patients undergoing CLND was significantly higher with regard to overall wound complications compared with patients with TLND. In these subgroups, POSSUM failed to predict the rates precisely.

CONCLUSIONS The POSSUM score predicted the morbidity of the total patient group accurately but failed to predict the rates in the TLND and CLND subgroups. Patients receiving CLND showed the highest morbidity rates. Preoperative sentinel lymph node biopsy therefore has more influence on postoperative morbidity than the physiological parameters represented in the POSSUM physiological score.

KEYWORDS

Melanoma – Lymph node dissection – Operative risk – POSSUM

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When lymphatic metastasis occurs, surgery is the primary treatment modality in melanoma patients. Patients undergo elective, therapeutic and palliative dissection. For patients with localised melanoma and clinically uninvolved lymph nodes, a sentinel lymph node biopsy (SLNB) has become the standard care.^{1,2} If micrometastases are detected in the sentinel lymph node (American Joint Committee on Cancer [AJCC] stage III A/B), a completion lymph node dissection (CLND) is recommended.⁵ For patients with clinically detectable (macroscopic) nodal metastasis (AJCC stage III B/C), a therapeutic lymph node dissection (TLND) is recommended. In a recurrent and extensive nodal disease status or with an advanced metastatic melanoma (AJCC stage IV), it is recommended that patients receive a palliative lymph node dissection in order to obtain local disease control (LDC) and optimise quality of life.

While TLND is curative in 25–50% of patients with macroscopic tumour masses, the survival benefit in CLND patients has not yet been proved. Currently, the value of CLND is being evaluated by controlled studies; results will not be available for another few years due to the large number of cases needed. Meanwhile, the potential morbidity of the procedure must be weighed against the value of prognostic information gained from performing SLNB.^{4–8}

While SLNB is a minimally invasive procedure with limited morbidity, CLND and TLND are reported to be associated with considerable complication rates from 19.9% to 51%. There are several reports on factors influencing the morbidity rates such as the site of lymph node dissection (groin or axillary) and the body mass index (BMI) of the patients as well as the number of tumour-affected lymph nodes.^{9–15} However, the reported morbidity rates are mostly based on multiple retrospective single institutional trials

Table 1 POSSUM physiological subscore¹⁵

Score	1	2	4	8
Age (years)	<60	60–70	>70	
Cardiac signs	No failure	Diuretic, digoxin, anti-anginal or hypertensive therapy	Warfarin therapy, peripheral oedema, borderline cardiomegaly	Raised jugular venous pressure, cardiomegaly
Respiratory history	No dyspnoea	Mild COAD, dyspnoea on exertion	Moderate COAD, limiting dyspnoea (one flight)	Dyspnoea at rest (rate >30/min); fibrosis or consolidation
Electrocardiogram	Normal		Atrial fibrillation, (rate 60–90 beats/min)	VES > 5/min, Q waves or ST/T wave changes, any other abnormal rhythm
Blood pressure (mmHg, systolic)	110–130	131–170 or 100–109	>170 or 90–99	< 89
Pulse (beats/min)	50–80	81–100 or 40–49	101–120	>120 or <40
Haemoglobin (g/dl)	13.0–16.0	11.5–12.9 or 16.1–17.0	10.0–11.4 or 17.1–18.0	<10.0 or >18.0
White cell count (x 10 ³ /μl)	4.0–10.0	10.1–20.0 or 2.1–4.0	>20.0 or <3.0	
Potassium (mmol/l)	3.5–5.0	3.2–3.4 or 5.1–5.3	2.9–3.1 or 5.4–5.9	<2.8 or >6.0
Creatinine (mg/dl)	<0.84	0.85–1.13	1.14–1.69	>170
Sodium (mmol/l)	>136	131–135	126–130	<125
Glasgow coma scale	15	12–14	8–11	<8

and vary widely.¹⁴ Crude rates of morbidity and mortality after radical lymph node dissection do not allow an objective interpretation because the case mix and fitness of patients are not appropriately considered. Auditing instruments are therefore required for a critical evaluation of treatment outcome and quality of care.

The Physiological and Operative Severity Score for the enumeration of Mortality and morbidity (POSSUM) is a well established scoring system for predicting postoperative mortality and morbidity in general surgery. POSSUM was created for surgical auditing by Copeland *et al* between 1989 and 1991 at Walten Hospital, Liverpool, UK.¹⁵ It was shown in patients treated in a general surgery department that the POSSUM scoring system predicted morbidity and mortality rates similar to the observed rates. Over the years, the accurate prognostic capability of the POSSUM score and its practicability in varying surgical procedures has been confirmed, even in related fields beyond visceral surgery such as orthopaedics, vascular surgery and urology.^{16–20} Recently, our group demonstrated that POSSUM scores are useful for preoperative risk evaluation prior to surgery for complicated peptic ulcer disease and cholangiocarcinoma.^{18,21}

The aim of the current study was to evaluate the impact of POSSUM analysis in the postoperative morbidity and operative risk assessment of melanoma patients undergoing CLND and TLND.

Methods

The medical records of patients with cutaneous melanoma who underwent a radical lymph node dissection (RLND) at the Department of General Surgery and Thoracic Surgery at the University Hospital of Kiel from 1985 to 2008 were analysed retrospectively.

Radical lymph node dissection

RLND was performed as CLND for positive sentinel lymph nodes in accordance with German melanoma guidelines.²² For patients with clinically detectable metastatic disease of regional lymph nodes (AJCC stage III B/C), TLND was performed. AJCC stage IV melanoma patients with recurrent tumour disease or a palpable tumour mass received a palliative lymph node dissection or tumour debulking procedure for LDC. We performed either axillary or groin lymph node dissection depending on the SLNB sites.

Groin dissection included superficial and deep lymphadenectomy, in which the femoral-inguinal lymph nodes and the lymph nodes along the iliac artery and vein were excised, together with the obturatoric lymph nodes. The pelvic nodes were approached extraperitoneally through a lower abdominal wall incision following the technique described by Baas *et al*.²⁵ Axillary dissection comprised dissection of levels I–III.

All procedures were performed with a standardised technique using a combination of electric cauterisation and ligation of the lymph vessels. No other vessel sealing systems were applied. All patients had closed suction wound drainage afterwards.

POSSUM score

The POSSUM scoring system consists of a physiological and an operative subscore (Tables 1 and 2). The physiological subscore comprises 12 preoperatively assessed parameters: age, cardiac signs, respiratory history, electrocardiogram, blood pressure, pulse, haemoglobin, white cell count, potassium, creatinine, sodium and Glasgow coma scale. Each of these factors is graded into four categories. The points awarded for each of the 12 factors are added up to attain the POSSUM physiological subscore.

The POSSUM operative subscore consists of six variables that are also classified into four grades: operative severity, number of procedures, blood loss, peritoneal soiling, presence of malignancy and mode of surgery. The points awarded for these six factors were also added and formed the POSSUM operative subscore. The subjective estimation of the operative severity was standardised to 'moderate' to keep controlled conditions. Both subscores were entered

into the complete score formula (Table 3) to assess the morbidity rates (complications).¹⁵

Defining complications

Wound infections were classified according the US Centers for Disease Control and Prevention criteria as superficial incisional, deep incisional, organ and space infections. Superficial incisional wound infections were limited to the subcutaneous fat whereas deep incisional infections invaded muscle or fascia (or both).^{24,25} A wound haematoma was defined as an accumulation of blood following a lymphadenectomy requiring surgical intervention. A seroma was defined as a palpable or ultrasonography-detected fluid collection at the lymphadenectomy site requiring aspiration, reinsertion of a drainage tube or surgical reintervention. Delayed wound healing was defined as whenever primary wound healing was not achieved within 14 days after primary surgery, irrespective of the cause (wound infection, skin flap necrosis, persistent discharge of lymphatic fluid). Our overall wound complication rate therefore composed wound infections, delayed wound healing, haematomas and seromas. Systemic complications were also recorded for the cardiovascular system, urinary tract and pulmonary system.

Statistical analysis

Data were entered into a statistical analysis database. Analysis was performed using SPSS® v13 (SPSS Inc, Chicago, IL, US). Univariate analysis was calculated using the chi-square test for categorical endpoints, the Mann-Whitney U test for continuous endpoints and a logrank test for survival endpoints. Results were deemed statistically significant with *p*-values of ≤ 0.05 .

Results

Patient characteristics and survival

The data for the overall study population are displayed in Table 4. There were 143 patients (59 male, 84 female) with a mean age of 58.1 years (range: 20–89 years). Of these, 52 patients required CLND, 84 TLND and 7 LDC. The mean hospital stay was 9.2 days (range: 2–37 days). No patients died within 30 days of surgery and so the operative mortality rate was 0%.

The median follow-up duration was 33 months. The median overall survival time of the entire cohort was 28.3 months. The median overall survival time in the CLND group was 43 months (range: 6–96 months), for the TLND group it was 27 months (range: 5–270 months) and for the LDC group 15 months (range: 9–34 months). The median progression-free survival time was 12.8 months (CLND: 31.5 months, range: 2–96 months; TLND: 7 months, range: 1–270 months; LDC: 0 months).

Morbidity and mortality

Complications are summarised in Table 5. The overall complication rate was 28.0%. There were only a few systemic complications (pneumonia and urinary tract system infections). Most of the complications occurred in the surgical region, resulting in an overall wound complication rate of

Table 2 POSSUM operative subscore¹⁵

Score	1	2	4	8
Operative severity	Minor	Moderate	Major	Major+
Multiple procedures	1		2	>2
Total blood loss	≤100ml	101–500ml	501–1,000ml	>1,000ml
Peritoneal soiling	None	Minor (serious fluid)	Local pus	Free bowel content, pus or blood
Presence of malignancy	None	Primary only	Nodal metastases	Distant metastases
Mode of surgery	Elective		Emergency resuscitation possible in >2h, surgery in <24h after admission	Emergency (surgery needed in <2h)

Table 3 POSSUM formulas for morbidity and mortality¹⁵

Morbidity	$\ln R / (1 - R) = -5.91 + (0.16 \times \text{physiological score}) + (0.19 \times \text{operative score})$
Mortality	$\ln R / (1 - R) = -7.04 + (0.13 \times \text{physiological score}) + (0.16 \times \text{operative score})$

25.9%. There were 21 wound infections (14.7%) with 15 superficial incisional infections (10.5%) and 6 deep incisional infections (4.2%). There were no organ or space infections. The most common complications were delayed wound closure (25.9%), surgical reintervention (aspiration, drainage) (17.5%), wound infection (14.7%) and seroma (10.5%).

Other reported factors influencing the incidence of complications are shown in Table 6. In our study, the number of dissected lymph nodes, percentage of affected lymph nodes and anatomical site of surgery (axilla) influenced the morbidity, with significantly fewer patients developing complications. Interestingly, BMI, POSSUM score and POSSUM physiological subscore had no significant impact on the development of complications (shown below).

Overall wound complication rates were significantly different between CLND (40.4%) and TLND (21.4%) patients ($p=0.04$). Furthermore, the developed complications were significantly more frequent in the CLND group than in the TLND group (delayed wound closure: 38.5% vs 19.0%, $p=0.04$; wound infection: 25.0% vs 8.3%, $p=0.03$; seroma: 15.4% vs 7.1%, $p=0.05$) (Table 5). The actual mortality rate was 0% whereas the rate estimated by POSSUM was 8.3%.

POSSUM morbidity estimations

POSSUM physiological and operative subscores were calculated for each of the 143 patients. Figure 1 shows an overview of the mean POSSUM physiological subscores of all patients together as well as separated for the CLND and TLND groups. The POSSUM (ie predicted) morbidity rate for all patients together was 32.9% and the observed morbidity for all patients was similar at 28.0% (Fig 2). The estimated morbidity rates were 21.9% in CLND patients, 39.3% in TLND patients and 43.4% in the LDC patients. The observed rates differed for all three patient subgroups (CLND: 38.5%, TLND: 19.0%, LDC: 14.3%).

Discussion

Regional lymph node metastases from primary melanomas commonly involve the cervical, axillary or inguinal node basins. Resection of the inguinal lymph node basin is associated with the greatest operative morbidity. The addition of deep groin dissection, including iliac, hypogastric and obturatoric lymph nodes increases the risk of additional complications.^{15,26,27} Several strategies have been discussed to minimise the morbidity associated with inguinal lymphadenectomy, ie the shape of the skin incision (parallel to the inguinal ligament vs S-shaped), sacrifice or preservation of the long saphenous vein, transposition of the sartorius muscle and preparation of a musculocutaneous flap.^{28–32}

We observed a higher morbidity rate after inguinal lymph node dissection (48.0%, Table 6). In various reports there are complication rates of between 25% and 90%.^{15,23,33,34} Dissection of the axillary region has been shown to be associated with a lower complication rate ranging from 4.6% up to 51%.^{12,35,36} In our study, the complication rate for axillary dissection was 23.5%.

The reported morbidity rates are mostly based on multiple retrospective single institutional trials (as are ours) and vary widely. It is therefore extremely difficult to make meaningful comparisons between the results from different institutions. Auditing instruments for the objective evaluation and comparison of treatment outcome and quality of care in different hospitals is becoming increasingly relevant. It is claimed that POSSUM can randomise the variety inherent to such a mixture of cases and can therefore predict morbidity and mortality rates accurately regardless of surgical procedure.^{15,37,38} It has been applied in a variety of surgical disciplines such as in urology, visceral and vascular surgery^{39,40} with opening of the abdominal cavity but also in non-abdominal interventions such as transurethral uro-

Table 4 Patient characteristics

	Overall	CLND	TLND	LDC
Number of patients	143 (100%)	52 (36.4%)	84 (58.7%)	7 (4.9%)
Age (years)				
Mean	58.1	52.4	61.4	67.9
Range	20–89	20–81	25–89	43–78
Sex				
Male	84 (58.7%)	27 (51.9%)	53 (63.1%)	4 (57.1%)
Female	59 (41.3%)	25 (48.1%)	31 (36.9%)	3 (42.9%)
Body mass index (kg/m²)				
Mean	26.1	25.7	26.3	26.2
Range	18.0–38.4	19.3–38.4	18.0–38.0	20.8–32.3
Localisation of primary tumour				
Extremity	71 (49.7%)	29 (55.8%)	39 (46.4%)	3 (42.9%)
Trunk	53 (37.1%)	22 (42.3%)	29 (34.5%)	2 (28.6%)
Unknown	19 (13.2%)	1 (1.9%)	16 (19.1%)	2 (28.6%)
Primary tumour type				
Nodular melanoma	71 (49.7%)	34 (65.4%)	33 (39.3%)	4 (57.1%)
Superficial spreading melanoma	23 (16.1%)	8 (15.4%)	15 (17.9%)	
Acrolentiginous melanoma	10 (7.0%)	2 (3.8%)	8 (9.5%)	
Not specified	39 (24.2%)	8 (15.4%)	28 (33.3%)	3 (42.9%)
Clark level				
II	2 (1.4%)	14 (26.9%)	2 (2.4%)	
III	36 (25.2%)	36 (69.2%)	22 (26.2%)	
IV	77 (53.9%)	2 (3.8%)	39 (46.4%)	2 (28.6%)
V	7 (4.9%)		3 (3.6%)	2 (28.6%)
Unknown	21 (14.7%)		18 (21.4%)	3 (42.9%)
Ulceration of primary tumour	56 (39.2%)	24 (46.2%)	31 (36.9%)	1 (14.3%)
Breslow's depth				
0.10–0.99mm	16 (11.2%)	2 (3.8%)	14 (16.7%)	
1.00–3.99mm	77 (53.8%)	37 (71.2%)	38 (45.2%)	2 (28.6%)
≥4.00mm	29 (20.3%)	13 (25%)	14 (16.7%)	2 (28.6%)
Unknown	21 (14.7%)		18 (21.4%)	3 (42.9%)
Localisation of lymph node dissection				
Groin (ilioinguinal)	75 (52.4%)	29 (55.8%)	41 (48.8%)	5 (71.4%)
Axilla	68 (47.6%)	23 (44.2%)	43 (51.1%)	2 (28.6%)
Number of lymph nodes excised (mean/range)	12.1 (1–45)	12.9 (2–14)	11.5 (1–45)	14.4 (3–23)
Number of tumour positive lymph nodes (mean/range)	2.7 (0–18)	1.0 (0–4)	3.4 (1–24)	8.2 (3–18)
Wound catheter suction in days (mean/range)	9.0 (1–37)	9.3 (1–37)	9.2 (1–23)	3.9 (2–10)
Mean hospital stay in days (mean/range)	9.2 (1–44)	10.4 (3–44)	8.6 (1–33)	6.7 (3–15)

CLND = completion lymph node dissection; TLND = total lymph node dissection; LDC = local disease control

Table 5 Early operative morbidity

	Overall	CLND	TLND	LDC	p-value*
Total complications	40 (28.0%)	21 (40.4%)	18 (21.4%)	1 (14.3%)	0.04
Overall wound complication rate	37 (25.9%)	20 (38.5%)	16 (19.0%)	1 (14.3%)	0.04
Delayed wound closure	37 (25.9%)	20 (38.5%)	16 (19.0%)	1 (14.3%)	0.04
Reintervention	25 (17.5%)	12 (23.1%)	12 (14.3%)	1 (14.3%)	NS
Wound infection	21 (14.7%)	13 (25.0%)	7 (8.3%)	1 (14.3%)	0.03
Seroma	15 (10.5%)	8 (15.4%)	6 (7.1%)	1 (14.3%)	0.05
Oedema	14 (9.8%)	8 (15.4%)	6 (7.1%)	1 (14.3%)	NS
Skin flap problems	8 (5.6%)	5 (9.6%)	2 (2.4%)	1 (14.3%)	NS
Abscess	7 (4.9%)	4 (7.7%)	3 (3.6%)	0 (0%)	NS
Haematoma	4 (2.8%)	2 (3.8%)	2 (2.4%)	0 (0%)	NS
Lymph fistula	3 (2.1%)	0 (0%)	3 (3.6%)	0 (0%)	NS

CLND = completion lymph node dissection; TLND = total lymph node dissection; LDC = local disease control; NS = not significant

*p-values refer to CLND vs TLND

Table 6 Possible risk factors affecting morbidity

	Patients with complications	Patients without complications	p-value
Mean number of dissected lymph nodes	16.4	10.8	0.02
Percentage of affected lymph nodes	35.1%	26.7%	0.021
Dissected lymph node region:			
• Axilla	16 (23.5%)	52 (76.5%)	0.04
• Groin (ilioinguinal)	36 (48.0%)	39 (52.0%)	NS
Body mass index	26.0kg/m ²	25.8kg/m ²	NS
POSSUM score	31.4	29.5	NS
POSSUM physiological subscore	17.3	16.9	NS

NS = not significant

logical resections, elective orthopaedic and neurosurgical procedures.^{40–42}

To our knowledge, the use of POSSUM in patients with malignant melanomas undergoing regional lymph node dissection has not yet been reported. The predicted morbidity rate for all patients was 32.9%, which is close to the observed rate of 28.0%. These complications included those that were systemic as well as wound related. Our morbidity rate is comparable with other studies on surgery for melanoma with reported rates of 19.9% to 51%.^{9–15} However, these reports do not provide further patients' details except the primary tumour stage and, in some cases, the height, body weight and BMI. Other possible risk factors such as concomitant diseases are not mentioned.

As shown in Table 6, the BMI did not alter the morbidity significantly. Moreover, the study population itself was quite homogenous with a mean BMI of 26.1kg/m² (range: 18.0–38.41kg/m²). It is well known that the region of lymph

node dissection, the number of resected lymph nodes and the percentage of affected lymph nodes are of major importance in developing postoperative complications.^{11,12} Besides the location of the dissected region as a risk factor, we confirmed that the number of resected lymph nodes and the percentage of affected lymph nodes influenced the complication rate significantly (Table 6). By using the POSSUM physiological subscore, which reflects the preoperative patient's status independently of the melanoma location and stage, we were able to characterise our patient cohort more objectively (Fig 1).

In this study, POSSUM did indeed predict the morbidity of the total patient group independently from tumour-specific characteristics such as location and dimension. However, by further analysis of the different treatment groups (CLND and TLND), it seems that interventions performed prior to the lymph node dissection (as in CLND patients with preoperative SNLB) have a more distinctive impact on the

postoperative course and, thus, reduce the predictive value of POSSUM, as shown below.

Separated morbidity for CLND/TLND patients

While SLNB is a minimally invasive procedure with low complication rates of approximately 4.6%,⁴⁵ the surgical completion of the regional lymph node region after SLNB is reported to be a procedure with a much higher morbidity. Furthermore, patients with a palpable tumour mass as a sign of advanced disease or even a recurrent tumour after a previous lymph node dissection are reported to have the highest morbidity rates.⁴⁴ The predicted morbidity rates in our patient population calculated by the POSSUM score were in line with those reported in the literature: the lowest morbidity was expected for the CLND group (21.7%) and the highest morbidity for the LDC group (43.4%) (Fig 2).

Moreover, focusing on the preoperative patient's status in our study cohort in order to identify high-risk patients before surgery (indicated by the POSSUM physiological subscore), the CLND patients seemed to be in a better physiological condition with a mean POSSUM physiological subscore of 15.1 compared with TLND patients (mean: 17.7) and LDC patients (mean: 19.3). Interestingly, other risk factors such as BMI, diabetes mellitus, other concomitant disease and region of the lymph node dissection did not differ significantly (Tables 4 and 5).

Surprisingly, the observed morbidity rates of the patients in the CLND and TLND groups were directly opposed to the predicted morbidity rates. While only 21.4% of the TLND patients developed at least one complication (systemic complications included), there was a morbidity rate of 40.4% in CLND patients. Complications differed particularly in the overall wound complication rate (19.0% TLND vs 38.5% CLND), resulting in a higher wound infection rate, development of seromas, abscesses, skin flap problems, oedemas and delayed wound closure (Table 5). The CLND and TLND groups did not differ significantly regarding the region operated on (groin vs axilla).

Nevertheless, our data seem to confirm observations of other groups where some authors report increased morbidity rates in CLND (after SLNB) compared with patients undergoing TLND. However, the reason for the elevated morbidity rates has not been shown clearly. Some authors argue that the pre-surgery itself increases the possibility of complications since the wound healing (even after a laparoscopic procedure) has not finished at the time of CLND. In our study, the average time interval between SLNB and CLND was 33 days and it did not have a significant impact on the course of complications. (Data not shown.) There might be other factors affecting the postoperative outcome.

In fact, the type of the cutaneous incision during SLNB is of major importance: if it is located within the surgical approach of a potentially following CLND, the tissue and scar could be removed easily later on. Thus, no curved skin incisions become necessary, which can possibly cause skin flap problems. This circumstance requires close cooperation with the performing SLNB surgeon (in the case of SLNB being carried out in a different surgical unit). Spillane *et al* reported a pilot study of a minimal access groin dissection

technique using an incision of 3–6cm in length.⁴⁵ Another possible explanation for the high morbidity rate of CLND after SLNB might be the initiation of systemic therapy by interferons or other substances after a positive SLNB prior to CLND. However, this particular effect could not be observed in our patient population. (Data not shown.)

Limitations of our study include the relatively small number of patients and the retrospective design. Prospective, larger numbered study designs are necessary for identifying other risk factors and evaluating new surgical techniques.

Conclusions

The POSSUM scoring system was not useful in predicting the morbidity rates in patients undergoing CLND or TLND for metastatic melanomas: the predicted and observed morbidity rates differed considerably. Patients with SLNB prior to CLND showed the highest morbidity rates although these patients were in minor stages of disease and in better physical condition preoperatively than those undergoing TLND or LDC.

In the future, it will be necessary to determine other preoperative parameters that might have an impact on the postoperative course. As soon as these parameters are identified, further prospective studies may answer the question as to whether POSSUM has to be modified or whether a new scoring system might be necessary.

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