Annals of Medicine and Surgery 60 (2020) 587–591

Contents lists available at ScienceDirect

Annals of Medicine and Surgery

journal homepage: www.elsevier.com/locate/amsu

Cohort Study

Two-phase amputation among critically ill patients with ischemic gangrene of lower limbs as a way to improve treatment outcome. Cohort study

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ARTICLE INFO

Keywords:
Amputation
Complications
Disarticulation
Gangrene
Mortality
Preoperative comorbidities
Reamputation

ABSTRACT

Background: The results of lower limb amputation, especially in critically ill patients with severe endogenous intoxication, sepsis, multi-organ failure and severe concomitant diseases are still unsatisfactory. Guillotine amputation is a method routinely used to reduce wound complications associated with wet gangrene and severe cases of diabetic foot, however, it is unclear how well it could help to decrease mortality and improve functional outcome when dealing with critically ill patients.

The objective: of the study was to estimate the effectiveness of two-phase method of urgent low limb amputation among critically ill patients with high risk of complications. The effectiveness was evaluated in terms of peri-operative mortality, frequency of early complications and ultimate level of limb loss.

Materials and methods: Two cohort groups of patients with acute lower limb gangrene were retrospectively matched. Approximately 25.8% of patients from the comparison (control) group (N = 240) died without surgery due to severity of their condition and ineffective pre-operative treatment. The remaining patients underwent one-phase high-level amputation after 48–72 h of pre-operative intensive care. The experimental group consisted of 153 patients who underwent guillotine amputation at the lower part of tibia (34.6%), knee disarticulation (32.0%), or open thigh amputation (33.3%), depending on the level of irreversible soft tissue necrosis. The reamputation with the stump shaping was performed later when their health status improved.

Results: The assessment of treatment outcomes showed that the two-phase amputation in critically ill patients (i) decreased the mortality from 48.7 to 37.9%, (ii) reduced the risk of wound complications from 20.9 to 11.1%, and (iii) improved functional results by saving the knee joint in 34.6 versus 4.5% in comparison/control group.

Conclusion: The method of two-phase amputation is recommended for critically ill patients.

1. Background and rationale

Despite the recent advances of modern vascular surgery, amputation of lower extremities due to critical ischemia remains one of the most frequent operations, and patients with the lower limb gangrene constitute a significant proportion of all surgeries. This amputation is one of the oldest established operations, however, it is still associated with frequent early postoperative complications and mortality, as well as with unsatisfactory long-term functional results [1,2].

The most severe cases are observed in elderly people with widespread wet gangrene due to obliterating vascular disease, decompensation of background diseases, sepsis and multiple organ failure. Over the past decades, the general trend in traumatology and oncology has been to perform organ-preserving operations, significantly reducing high-level lower limb amputation in patients with diabetic foot syndrome. Currently, the main indication for amputation of the lower extremities in most patients is critical ischemia caused by insufficiency of the peripheral arteries [1].

However, several issues remain without clear solutions, namely how to (i) lower the amputation level in patients with distal limb gangrene against the background of high occlusion of main arteries; (ii) reduce the number of early post-operative complications and related reamputations; (iii) decrease the postoperative mortality in critically ill patients undergoing amputations; and (iv) improve functional results by increasing the number of prosthetic limbs in patients with obliterating vascular diseases of the lower extremities.

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https://doi.org/10.1016/j.amsu.2020.11.045
Received 30 October 2020; Received in revised form 13 November 2020; Accepted 14 November 2020
Available online 24 November 2020

One way to address these issues, as well as to preserve the knee joint in patients with limb-threatening ischemia is to perform the amputation in two phases. The two-phase amputation is usually a last resort solution under severe clinical conditions, it is accompanied by high operational risk in patients with infectious and/or toxic shock, multiple organ failure, or the decompensation of concomitant diseases.

The goal of the first phase of surgery is to eliminate the source of endogenous intoxication by guillotine amputation of the infected part of the limb. The second phase of planned re-amputation with the formation of a stump is based on (i) assessment of the need, feasibility, timing, (ii) effectiveness of conservative treatment, (iii) the possibility of compensating for background and concomitant diseases, (iv) severity of wound infection, and (v) the degree of anesthetic risk. This approach is widely used in various medical institutions, but to our knowledge, no publications have objectively assessed the effectiveness of this tactic for critically ill patients.

2. Goal

The aim is to evaluate the effectiveness of two-phase surgical treatment in patients with indications for urgent high amputation of the lower limb who are at high anesthetic risk, early postoperative and infectious complications.

3. Methods

The trial is fully compliant with STROCSS criteria [3].

The work has been registered at the International Clinical Trials Registry Platform (ICTRP) with a Research Registry reference number ISRCTN12604387 (URL: http://isrctn.com/ISRCTN12604387).

4. Study design

The work was performed as an observational retrospective non-randomized controlled study of a continuous cohort.

5. Inclusion criteria

The criterion for patient inclusion in the study was the need to perform urgent (within 72 h after admission to the hospital) high amputation of the lower extremities with critical limb ischemia and severe or extremely severe condition. The indication for amputation was gangrene accompanied by progressive infection of soft tissues or a syndrome of endogenous intoxication caused by ischemic damage to the muscle tissue of the limb.

CRITERIA FOR NON-INCLUSION IN THE STUDY (exclusion criteria):

1. Patients with surgical soft tissue infection but without occlusion of the main arteries (including patients with extensive soft tissue infection due to a neuropathic form of diabetic foot syndrome).
2. Patients with pre-planned indications for amputation (including those operated within 72 h after admission), e.g., chronic critical ischemia and gangrene of the limb accompanied with unsuccessful or impossible angiosurgical intervention.
3. Patients with indications for urgent limb amputation occurring during their stay in the hospital.

5.1. Study setting

Patients of both groups were admitted to the hospital by ambulance with diagnosis of gangrene of the lower extremities. The main group consisted of 153 patients who were treated at the Surgical Department or the Intensive Care Unit (ICU) of the V.V.Vinogradov Moscow Municipal Hospital (Russia) from 2014 to 2018. Patients were selected by screening based on the need of high (above the ankle joint) limb amputation in the first 72 h from the moment of admission to the ICU. They comprised 13.2% of all patients admitted during this period with gangrene or trophic ulcers in the background of obliterating diseases of the lower limb arteries (1158 people in total).

As a comparison control group for the same indicator, 240 patients were selected retrospectively who were treated at the intensive care unit (ICU) and Surgical Departments of Moscow Municipal Hospital No. 53 (Russia) from 2008 to 2014. They accounted for 14.8% of all patients with gangrene or trophic ulcers in the background of chronic critical limb ischemia admitted during this period (1615 people in total).

5.2. Medical intervention

The comparison (control) group patients were admitted to the ICU of Moscow Hospital No. 53 for preoperative preparation in order to reduce the anesthetic risk, and then a standard amputation was performed with primary stump formation at the safest level. Preoperative preparation consisted of stabilization of hemodynamic parameters, correction of water-electrolyte disbalances and compensation of organ dysfunction. The preoperative preparation period was limited to 72 h. The intensive care was unsuccessful for a number of patients of the comparison group, they could not be stabilized, and they were not subjected to amputation due to severity of their condition. The remaining patients were subjected to one-phase limb amputation with primary simultaneous stump formation. The level of amputation depended on the level of occlusion of the main arteries and the spread of necrotic, ischemic and inflammatory changes of soft tissues.

In the main group, the only contra-indication to surgery was extremely severe condition corresponding to the 5th degree of anesthesiological risk by classification of the American society of anesthesiologists (ASA physical status classification system). Preoperative preparation was limited to stabilization of hemodynamic parameters and correction of severe water-electrolyte disorders. Next, a guillotine amputation of the limb aimed at eliminating the source of endogenous intoxication was performed under intravenous, conductive or spinal anesthesia. Depending on the level of irreversible soft tissue deterioration, guillotine amputation was performed at the level of lower leg, exarticulation at the knee joint, or at the hip level. Usually, operations continued from 10 to 20 min, and the loss of blood was minimal.

After patient stabilization, elimination of signs of infection, and compensation of background and concomitant conditions, the reamputation of the limb was performed at the optimal level with the formation of a stump.

5.3. Outcome of the study

To assess the effectiveness of two-phase limb amputation approach, the following indicators were analyzed.

The primary endpoint of the study was the level of hospital mortality in the two groups of patients.

The level of amputation, duration of hospitalization, and frequency of postoperative wound complications including repeated surgical interventions, were used as **secondary endpoints.**

5.4. Analysis in subgroups

The characteristics of patients in both groups are presented in Table 1.

As shown in Table 1, both demographic indicators and presence of concomitant diabetes mellitus were similar for the two groups of patients. Diabetes was observed in significant number of cases, however, as noted previously, patients with the infected neuropathic form of diabetic foot were not included in this study.

The distribution of patients by the time of performed primary (first phase) amputation is shown in Table 2.

As shown in Table 2, majority of patients in the main group were

Table 1
Demographic indicators and frequency of Diabetes mellitus in groups of patients.

	Main group		Comparison group		Statistical value
Number of patients	153		240		
Age	74,2 ± 7.1		73,5 ± 10.4		p = 0.96[a]
Sex	N	%	N	%	
M	96	62.7	138	57.7	ξ2 = 0.27[a]
F	57	37.3	102	42.3	ξ^2 = 0,46[a]
Diabetes mellitus	46	30.1	58	24.3	ξ^2 = 1.61[a]

[a] - The difference is not statistically significant at α = 0.05.

Table 2
Distribution of patients by the time of primary amputation.

	Main group (N = 153)		Comparison group (N = 240)		ξ^2
Timing of amputation					
	N	%	N	%	
On the day of admission	54	35.3	9	3.8	68.75[a]
On 24–48 h	64	41.8	62	25.9	10.8[a]
On 48–72 h	35	22.9	107	44.8	19.36[a]
Not operated due to severity of general condition	0	0	62	25.8	76.01[a]

[a] - The difference is statistically significant at α = 0.05.

operated in the first 48 h after admission. In the comparison group, amputation was frequently performed on the third day after admission. In addition, in one quarter of cases (25.8%), attempts to stabilize the patient condition and lower the risk of surgery were unsuccessful, thus the patients were considered inoperable, and all of them died within 4 ± 0.7 days.

5.5. Statistical analysis

The sampling size was estimated according to the method of M. Bland [4] as 140 observations. Comparison of treatment results by groups was performed using the Pearson ξ2 criterion, the Fisher exact criterion, and the Student's t-test with a significance level of 0.05 (Excel statistical package).

6. Results

Analysis of the treatment results between the two groups elucidated significant differences in the level of performed amputation (Table 3).

In the majority (95.5%) of the comparison group, the above-knee amputation was chosen as a "safe" level. In the main group, the first step was to remove a clearly non-viable part of the limb without forming a stump and applying stitches to the wound. This allowed to control condition of the stump tissues and minimize the risk of purulent complications. This conservative approach made it possible to end up with the below-knee amputation in every third case, thus preserving the knee joint. However, if the necrosis zone spreaded to the entire lower leg, disarticulation in the knee joint was chosen as the preferable amputation level. In these cases, guillotine amputation was performed above the zone of soft tissue necrosis at the level of visually determined signs of muscle viability (visual presence of bleeding and contractility).

Table 3
Distribution of operated patients according to the level of amputation.

Level of Amputation	Main Group N = 153		Comparison Group N = 178		ξ^2
	N	%	N	%	
Below-knee	53	34.6	8	4.5	69.52[a]
Knee disarticulation	49	32.0	0	0	87.48[a]
Above-knee	51	33.3	170	95.5	183.99[a]
Total number of amputations	153	100.0	178	100.0	

[a] - The difference is statistically significant at α = 0.05.

The main results of treatment are shown in Table 4. Although the postoperative mortality in the comparison group was lower (30.9 vs. 37.9%), this difference is not statistically significant. Furthermore, if to include non-operated patients, there is a significant decrease in overall mortality in the main patient group (37.9 vs. 48.9%).

In the comparison group, wound complications occurred in every fifth case (20.9%). The wound infection and myonecrosis of the stump were the main observations, together with less frequently observed hematomas and necrosis of the skin edges. Approximately one half of complications observed in the comparison group required repeated debridements, necrectomies or reamputation.

The decrease in frequency of wound complications was noticeable for the main group: they were documented in 11.1% of cases (Table 4). Usually they occurred due to overly distal level of guillotine amputation, resulting in spread of necrotic changes to the more proximal level, and requiring the debridement, necrectomy or reamputation.

Favorable outcome of the first phase in the main group resulted in the next stage: planning of re-amputation and stump formation based on the patient general condition, compensation for background and concomitant diseases and the associated anesthetic risk. During hospitalization, reamputation with stump formation was performed in 42 patients of the main group. Overall, 39 patients were discharged to the outpatient treatment with open stump wounds and recommended planned re-hospitalization for final phase of surgery.

7. Discussion

Doctors working in urgent care hospitals frequently encounter situations when a patient is admitted in extremely severe condition, while having acute cardiac or neurological pathology, sepsis, or a full set of decompensated chronic diseases, and needing emergency surgery. The rational way to proceed is to perform minimum required intervention that may not completely solve the problem, but instead can stop the acute disease manifestations, improve the general condition, and minimize possible thanatogenesis.

The optimal timing of surgery, the level of amputation and the decision on whether or not to shape the stump are difficult issues when dealing with patients who have massive ischemic necrosis of soft tissues of the limb, especially in the cases complicated by infection ("wet gangrene") and accompanied by hypovolemia, decompensation of circulatory failure, diabetes, cardiopulmonary failure, kidney failure, or sepsis and multi-organ failure. On one hand, performing complete amputation in the background of these conditions bears a significant anesthetic risk. On the other hand, continuous presence of a diseased limb works as a source of endogenous intoxication, thus, significantly complicating treatment of the underlying disease, conservative therapy

Table 4
Results of treatment.

	Main group		Comparison Group		ξ^2
General mortality	58	37.9%	117	48.9%	8.06[a]
Mortality of non-operated patients	–	–	62	100%	46.25[a]
Postoperative mortality	58	37.9%	55	30.9%	0.88[b]
Wound complication frequency	17	11.1%	50	20.9%	18.9[a]
The necessity of repeated debridements or reamputation	14	9.2%	26	10.9%	0.3[b]
Mean duration of hospital stay among survivors, days	16 ± 9.7		23 ± 14.2		p = 0.68[b]

[a] - The difference is statistically significant at α = 0.05.
[b] - The difference is not statistically significant at α = 0.05.

and preoperative preparation.

High limb amputation is a highly traumatic intervention, often accompanied by significant blood loss, especially in patients receiving antiplatelet therapy for obliterating limb artery disease or other cardiovascular conditions. The desire to reduce the risk of postoperative wound complications, such as wound suppuration and stump myonecrosis, frequently forces the surgeon to choose a higher level of amputation, which in turn increases surgical trauma [5]. In case of a favorable outcome, such operation worsens the functional result, useability of prosthetics and patient's quality of life.

These risks can be avoided by using the proposed two-phase amputation approach. An important issue is the level of primary amputation. It is selected based on the following requirements:

1. Completeness, i.e. removal of all non-viable tissue.
2. Minimum trauma by cutting off the limb in "muscle-free" zones (knee joint or the lower third of the shin).
3. Minimum duration of surgery to reduce the degree of anesthetic risk.

The small volume of intersected soft tissues at the lower leg and knee joint levels ensures a relatively short duration of the operation, minimum traumatic intervention and low intraoperative blood loss. A significant portion of the resulting wound surface is the articular surface of the femur bone (if disarticulation at the knee joint), or cross-section of tibia and fibula (with guillotine amputation of the lower third of the shin). This results in the minimum possible exudation from the wound in the postoperative period, and moderate pain syndrome. Removal of the necrotic and infected tissues at the first operation step reduces the soft tissue infection and makes possible to conduct examination and preparation for the 2nd operation. Despite the obvious advantages of two-phase amputation, this approach has not been widely discussed in the literature, and its effectiveness has not been adequately assessed.

Guillotine amputation has been used for more than a century in order to prevent wound complications, especially in military field surgery and in cases of severe trauma. The advantages of two-phase amputation in cases of severe infection leading to the loss of a limb have been documented in numerous studies. In a randomized study, Fisher et al. demonstrated a significant reduction in the number of wound complications, the reduced need for repeated surgical treatments, and significantly shorter duration of inpatient treatment associated with two-phase amputation [6]. Two-phase amputation is the method of choice in the cases of loss of foot support in patients with infected forms of diabetic foot [7,8]. However, the main indication for this type of surgery is the risk of infectious wound complications with wet gangrene, or massive traumatic injury to the limb. The use of this tactic is poorly documented for high surgical risk patients with critical ischemia accompanied with decompensation of background and concomitant diseases.

Meta-analysis of studies on the mortality after high amputations of the lower extremities indicates that multi-phase interventions provide additional risk for death, however, in many cases they become unavoidable with the development of complications [2]. At the same time, a recent publication of Silva et al. [9] has concluded that even in severe cases, the staged two-step amputation provides for a higher rate of technical success and lower mortality rates as compared to single intervention, which is consistent with our findings.

Disarticulation in the knee joint is sometimes used as the final phase of surgical treatment, but this mainly concerns traumatic amputations in young patients [10]. Adherents of this method point out the functional advantages associated with the stump supportability and preservation of the function of hip muscles [11]. However, disarticulation due to vascular insufficiency often results in impaired healing of the stump wound [12–15]. This consideration together with specifics of prosthetic usage make the knee disarticulation unpopular with surgeons, therefore, this surgery comprises only 1.7% of the total number of amputations [10]. Using disarticulation in the knee joint as the final level of amputation implies cutting out soft-tissue skin-fascial or skin-muscle flaps. If the primary suture is not applied to the wound, such approach will lead to formation of extensive wound surface with inevitable risk of secondary infection that may negate the advantages of two-phase amputation.

As an alternative to staged amputation, some authors describe 'physiologic cryoamputation' as a way to temporary reduce the resorption of endotoxins from ischemic and/or infected limb in critically ill patients [16]. This method is still not a common practice because hypothermia of non-viable tissues does not completely solve the problem of endotoxicosis, instead only allowing short delay of surgery that is often insufficient to stabilize patient's condition. Our findings suggest that two-phase amputation in difficult clinical situations is a reasonable approach, if it is performed as a part of complex treatment.

8. Strenghts and limitations

To our knowledge, this is the first study of two-phase amputation approach comparing different surgical tactics in the same contingent of patients in similar hospitals. The one-phase or two-phase amputations were a part of routine surgical practice. Two of the study authors participated in patient treatment and surgery in both hospitals. The obvious limitations of the work are its retrospective origin and significant time interval between the two analyzed patient groups. Thus, we could not establish whether considerable differences in intensive care existed between the groups.

9. Conclusion

This study is focused on analysis of patients with indications for urgent high amputation of the lower limb in the background of multiple organ failure, endogenous intoxication, sepsis, decompensation of preexisting diseases and high operational risk. Two groups of patients were treated in two clinical hospitals in Moscow in 2008–2014 (comparison group) and in 2014–2018 (main group). In the comparison group, the treatment consisted of preoperative preparation, followed by emergency amputation with primary stump formation. In most cases, surgery was performed 48–72 h after admission. A significant number of patients were found to be inoperable due to unacceptable anesthetic risk.

In the main group, the treatment consisted of stabilization of hemodynamics and correction of water-electrolyte disorders, followed by immediate guillotine amputation at the level of the lower third of the shin (34.6%), disarticulation at the knee joint (32.0%), or at hip level (33.3%), depending on the prevalence of irreversible changes in the soft tissues of the limb. Reamputation with stump formation at the optimal level was performed as planned surgery after stabilization of the patient condition and adequate preoperative preparation.

Recomendations

Analysis of treatment results shows that the use of two-phase amputation tactics reduced the mortality rate in the patients with extremely severe disease from 48.9 to 37.9%, decreased the number of postoperative wound complications from 20.9 to 11.1%, and improved the functional result by performing amputation below the knee joint in 34.6% of patients.

We suggest this tactic as a method of choice for critically ill patients with indication to immediate high-level lower limb amputation.

Provenance and peer REVIEW

Not commissioned, externally peer-reviewed.

Funding

Specific funding was not used for this study.

Conflicts of interest/Competing interests

Authors declare no conflicts of interest.

Availability of data and material

Data are available on request from Vitaly O.Tsvetkov (Tsvetkow@yandex.ru).

Code availability

ISRCTN12604387.

Authors' contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Vitaly O. Tsvetkov, Elena M. Gorshunova, Olga V.Kolovanova and Jury A. Kozlov, Vakhtang V. Gobedjishvili took significant part of material preparation and study management. The first draft of the manuscript was written by Vitaly O.Tsvetkov and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Registration and ethics

Research Registry number is ISRCTN12604387.

The trial was discussed with the Local Ethics Committee of the V.V. Vinogradov Moscow Municipal hospital. Given that the work is observational, carried out within the routine clinical practice and does not involve changes in the approved Health and Economic standards of the examination and treatment of patients, and data of the patients used in the study were completely impersonal, obtaining the informed consent of the patients was not required beyond the approved applications to the order No. 300, V.V.Vinogradov Moscow Municipal hospital from August 28, 2015.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2020.11.045.

Author disclosure form

Authors of article "Two-phase amputation among critically ill patients with ischemic gangrene of lower limbs as a way to reduce mortality and improve treatment outcome. Retrospective cohort trial" agree to publication in the Annals of Medicine and Surgery.

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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