



# Comparison of different durations of physical activity restrictions following incisional hernia repair in sublay technique, the 3N6 trial: A prospective clinical trial

Katherina R. Boettge<sup>a,\*</sup>, Roland Croner<sup>b</sup>, Rolf Lefering<sup>b</sup>, Eric Lorenz<sup>b</sup>, Christoph Paasch<sup>b,c</sup>

<sup>a</sup> No Insurance Surgery, 653 N Town Center Drive, 89144 Las Vegas, USA

<sup>b</sup> Department of General, Visceral, Vascular and Transplant Surgery, University Hospital Magdeburg, Leipziger Strasse 44, 39120 Magdeburg, Germany

<sup>c</sup> Department of General, Visceral and Cancer Surgery, Helios Klinikum Berlin-Buch, Schwanebecker Chaussee 50, 13125 Berlin, Germany

## ARTICLE INFO

### Article history:

Received 22 April 2020

Received in revised form 12 May 2020

Accepted 13 May 2020

Available online 23 May 2020

### Keywords:

Incisional hernia

Physical activity restrictions

Sublay technique

Physical rest

Recurrence rate

Chronic pain

## ABSTRACT

**Background:** Incisional hernias (IH) occur in 4 to 20% of cases following abdominal surgeries, often after laparotomies. In the US, there are 4 to 5 million laparotomies performed per year, which could lead to 400,000 to 1,000,000 IHs. Therefore, this disease accounts as an important social-economic factor. Furthermore, these hernias can lead to bowel incarcerations, chronic pain, and a decrease in quality of life. To guarantee sufficient wound healing and decrease the recurrence rate, physical activity restrictions (PAR) are recommended. The standard recommendations for PAR seem to vary from 0 to 12 weeks, but the evidence remains low due to a lack of clinical trials. Conducting the study at hand, we aim to provide more evidence on this topic.

**Methods:** The 3N6 trial will be conducted as a national multicenter prospective trial with two study groups (n = 90), where the goal is to find matched pairs within the two groups. Patients who underwent open incisional hernia repair (IHR) in sublay technique will be enrolled. A patient in the 3-week PAR group will be matched to a patient in the 6-week PAR group based on heavy lifting, male gender, BMI > 30, and large hernia > 7 cm. The primary endpoint is the duration of sick leave that patients require to return to work, by comparing PAR of 6 weeks with PAR of 3 weeks. The secondary endpoints are the recurrence rate, seroma formation, and chronic pain one year after surgery and postoperative complications within 30 days using Clavien-Dindo-classification.

**Dissemination:** The findings will be published in a peer-reviewed journal. We may also present the findings at local and/or national conferences.

Published by Elsevier Ltd on behalf of Surgical Associates Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. Introduction

Incisional hernias (IH) occur approximately in 4 to 20% of cases following abdominal surgeries, primarily after laparotomies [1]. In the US, there are 4 to 5 million laparotomies performed per year, which could result in the occurrence of an incisional hernia in 400,000 to 1,000,000 cases [2]. Therefore, incisional hernias account as an important economic factor. Furthermore, incisional hernias can lead to bowel incarcerations, chronic pain, and a decrease in overall quality of life. Risk factors for developing an

**Abbreviations:** IHR, Incisional hernia repair; IH, Incisional hernia; PAR, Physical activity restrictions, CHD, coronary heart disease; DVT, deep vein thrombosis, SD, standard deviation.

\* Corresponding author.

E-mail address: [katrinab.nis@gmail.com](mailto:katrinab.nis@gmail.com) (K.R. Boettge).

<https://doi.org/10.1016/j.isjp.2020.05.001>

2468-3574/Published by Elsevier Ltd on behalf of Surgical Associates Ltd.

This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

incisional hernia include postoperative wound infections, advanced age, obesity with a BMI > 30 kg/m<sup>2</sup>, chronic heart disease, diabetes, as well as a vitamin C deficiency [3–5]. The mentioned risk factors may lead to insufficient wound healing which results in a gap in the abdominal fascia and ultimately leads to the development of an incisional hernia.

There are various methods to repair IHs. They differentiate in terms of technique (open vs laparoscopic), the implementation of a mesh, and the mesh position (inlay vs sublay vs onlay vs underlay). The recurrence rate of these various techniques varies from 2 to 44 % [6–8].

To reduce this risk of recurrences as well as ensuring sufficient healing of the fascia with proper mesh ingrowth, postoperative physical activity restrictions (PAR) with avoidance of heavy lifting are frequently recommended. After conducting surveys among surgeons and patients, we revealed that the recommendations vary

from surgeon to surgeon from 0 to 12 weeks [9,10]. The different durations of PAR did not impact postoperative outcome. Moreover, a literature review on that topic did not yield any prospective trials. In summary, a clear time frame of physical rest is still missing [9,10].

Hence, we aim to provide more evidence because a shorter period of PAR after IHR could have a social-economic impact, as well as influence a patients' overall quality of life after IHR.

## 2. Methods

The 3N6 trial is conducted as a multicenter prospective pseudo-randomized trial with two study groups, where the aim is to find matched pairs within the two different groups. Matching criteria will be heavy weight lifting (yes/no), gender, BMI ( $\geq 30$  kg/m<sup>2</sup> /  $< 30$  kg/m<sup>2</sup>), and size of hernia.

Heavy weight lifting is defined as heavy work, such as carrying loads weighing up to 40 kilograms on the plain or climbing under medium loads and handling tools (over 3 kilograms in weight), including power tools with a strong recoil effect, shoveling, digging and hoeing.

The study is planned over a time period of 4 years within 4 different medical centers. We include an evaluation of patients over 1 year combined with a 1-year and 2-year follow-up.

The aim of this study is to evaluate whether physical activity restrictions of 3 weeks, including staying home from work, are a sufficient recovery time.

Physical activity restrictions consist of avoiding heavy weight lifting ( $\geq 10$  kg), abdominal muscle training in particular and no contact sport. Moderate bicycling, walking and running will be allowed.

A particular recovery program is not intended.

The trial has been ethically approved in April 2020 by the Ethics Committee of the University hospital Magdeburg (04–27–2020, ID 46/20), Germany. A study registration has been completed (German clinical trial registry; ID: DRKS0002102).

## 3. Objectives

The primary endpoint is the duration of sick leave that patients require either to return to work, or to resume their normal daily activities by comparing PAR of 6 weeks with PAR of 3 weeks. Hereby, we will keep the different work environments (Matching criteria; heavy weight lifting: yes or no) in mind, e.g. retiree, office worker, construction worker etc.

The duration of sick leave will be documented by a sickness certificate from the family doctor. The duration of this sickness certificate will be questioned during the second follow-up.

The secondary endpoints are postoperative complications within 30 days using Clavien-Dindo-classification [11], seroma formation, chronic pain, and the recurrence rate one and two years after surgery.

The recurrence rate after one year will be expected to be around 10%, which we expect to be equal in both groups. Our sample size is too small to find a significant difference in the recurrence rate in both study groups, and to prove a reasonable range of equivalence.

### 3.1. Design and setting of the study

The participants will be informed before their elective incisional hernia repair and the allocation will occur 1 to 2 days before the participants' discharge from the hospital.

The allocation will be set as a matched-pair process to increase the comparability of the groups. Therefore, the participants will be matched according to the following four criteria: (1) heavy weight lifting  $> 40$  kg yes/no, (2) male/female gender, (3) BMI  $\geq / < 30$ , and

(4) small/large hernia ( $\geq 7$  cm), which creates 16 different combinations. The first allocation within each subgroup will be the assignment to the 3-week PAR group. The next assignment in each subgroup will be to the 6-week PAR group. This will be continued in an alternate fashion within each subgroup. The study could therefore be described as a prospective matched-pair design, with a maximum number of potential pairs by alternating the allocation in each subgroup. Assignment will be organized centrally so that each participating medical center will mostly be unaware of the allocation of the next case (allocation concealment), except for the first few cases.

This approach will lead to the following results: within each of the 16 subgroups the number of participants receiving 3-week PAR will be equal or one more than the number of participants receiving 6-week PAR. This will create an optimal number of matched pairs for the subsequent analysis. It will increase the power of the study and compensates for the small sample size.

The study groups show the following characteristics:

- Group 1: 3-week PAR
- Group 2: 6-week PAR

### 3.2. Patient characteristics and recruitment

Eligible patients who underwent open incisional hernia repair (IHR) in sublay technique will be enrolled. They must be over the age of 18, not unemployed, consent to the participation in the study, and have an incisional hernia diameter  $> 2$  cm. A patient in the 3-week PAR group should have 4 similar characteristics as a patient in the 6-week PAR group. These characteristics include: Heavy lifting, male gender, BMI  $> 30$ , and large hernia  $> 7$  cm.

Exclusion criteria include the occurrence of DVT, pregnancy, a non-treated HIV infection, residence  $> 200$  km from the hospital, no working individuals

As quality assurance all patients were operated on by an experienced surgeon ( $> 10$  incision hernia repair/year).

### 3.3. Follow up

Patients who were allocated to the 6 weeks PAR group will be contacted by phone after 6 weeks. The patients will be asked to terminate the PAR.

Patients who were allocated to the 3 weeks PAR group will be contacted by phone after 3 weeks. The patients will be asked to terminate the PAR.

Individuals who stated that they terminated the PAR earlier than allowed (according to group allocation), will be counted as a drop out.

All patients will be contacted on 12 weeks after their surgery by phone to evaluate the duration of sick leave. The patients were asked to count the days on their sick leave certificate.

To further evaluate the secondary outcomes of the study, such as recurrence rate, the patients will return to the hospital after one year and two years after surgery to undergo physical examination, as well as an ultrasound of the former incisional hernia.

**Trial status:** The recruitment will begin on 08/01/2020. A study period of 4 years is estimated.

### 3.4. Statistical analysis

The aim of the study is the evaluation of two different lengths of PAR after IHR in sublay technique. The primary endpoint is the duration of sick leave that patients require either to return to work or to resume their normal daily activities, by comparing PAR of 6 weeks with PAR of 3 weeks. We expect that the duration of sick leave and therefore the return to work will be shorter after 3 weeks

PAR. Using paired data, we could prove a difference of half a standard deviation (SD) with  $2 \times 33$  patients, with  $\alpha = 0.05$  and 80% power (paired t-test). As we intend to analyze the data with a non-parametric rank test, (return-to-work data were assumed not to be normally distributed) the sample size must be increased by 10%, which corresponds to 36 pairs and thus 72 patients. Due to the randomization technique, nearly all patients will be able to be matched. An expected number of 8 to 10 cases might not be able to be matched. This would increase the required sample size to 80–82 cases. Finally, a 10% drop-out rate must be considered. This results in a total of 90 patients that need to be included.

The secondary endpoint is the recurrence rate after one year. We expect a recurrence rate of 10% in both study groups based on the following data:

Author:	Study design and enrolled patients:	Recurrence rate:
Helgestrand et al. 2013 [9]:	Prospective clinical trial (PCT); n=323	12.1%
Israëlsson et al. 2006 [10]:	National survey; n=123	7.3%
Kurmann et al. 2011 [11]:	PCT; n=56	17.9%
Raftopoulos et al. 2003 [12]:	Retrospective analysis; n=22	18%

The evaluation period will assess 80 patients. With this sample size, a proof of non-inferiority will not be feasible since the range of equivalence would be too large. To obtain statistical significance with a recurrence rate of 10% in both groups, it would require a recurrence rate of less than 15% in each group and ultimately a sample size of at least 800 patients (400 per group). Therefore, the recurrence rate will only be evaluated as a secondary endpoint.

The analysis will be made in the following manner:

- A. Comparison of groups: The data of the matched pairs will be analyzed. Through the matching process, we have an ideal comparison of the 4 criteria previously defined. The analysis of the 72 patients (36 vs. 36) will be made through analyzing dependent data (Wilcoxon rank sum test).
- B. 3-week PAR group: Through the pseudo-randomization process, we expect approximately 50 patients in the 3-week PAR group. With a recurrence rate of 10%, the 95% confidence interval would range between 3.2% and 23.3%, or, if a one-sided 95% confidence interval was used, the recurrence rate would be < 21%.

Furthermore, we are planning to continue the 3-week PAR group as a prospective observational study beyond the study period without any randomization to ultimately increase the statistical certainty regarding recurrence rates in this group.

### 3.5. Patient and public involvement

Patients were not involved in the design of this study, selection of outcome measures, development of research question, or in the recruitment to and conduct of this study. The burden of the intervention will be assessed during follow-up. A brief summary of the results will be made available in German or English to all patients on request.

## 4. Discussion

This study aims to optimize postoperative recommendations regarding physical activity restriction after IHR. The objectives of

the recommendations include a shortened recovery time that may have a positive impact on the duration of sick leave. The recommendation of PAR, including the limitation of heavy lifting after IHR has been implemented for a long period of time in postoperative care [9,10]. Bassini had already recommended in 1890 a period of PAR for 6 weeks following inguinal hernia repair [12]. Taylor et al. performed an RCT analyzing the data of 97 royal officers following open inguinal hernia repair. A correlation between the recurrence rate and a prolonged time of physical rest was not detected [13]. Therefore, it is possible that a shortened time of PAR may also have no negative impact following IHR, despite the differences in pathogenesis and treatment of inguinal hernias.

The concept behind PAR following IHR seems to be attributed to a sufficient time for proper wound healing, but mainly to prevent recurrences. There are no strict guidelines regarding the length of PAR, which leads to a variation between 0 to 12 weeks varying from surgeon to surgeon [9,10].

To that Majercik et al. showed in an animal model that the mesh implementation had already happened after only 2 weeks [14]. There are further studies that show a positive impact of early ambulation on cellular healing caused by a rapid increase of DNA and collagen synthesis [15]. Another randomized controlled trial showed a 2-year recurrence rate of 1.1% in 85 patients with IH that were repaired in inlay technique with a postoperative course of physical rest of 3 weeks [16]. In a study conducted by our department, we found that the postoperative outcome does not seem to improve with an extended time of PAR. Therefore, we assumed that a shortened PAR would be beneficial [8].

A recent study by Slim and Standaert lead to the conclusion that pre-operative prehabilitation referred to as enhanced recovery programs, as well as early mobilization, may be of great benefit. These programs include components such as tobacco cessation, obesity, diabetes and malnutrition management. It might be more important than prolonged postoperative PAR.

A review of literature by our study group did not reveal prospective trials analyzing the impact of prolonged physical rest and a late resumption of work on the clinical outcome following IHR.

The 3N6 trial is the first prospective trial to investigate a possible early return to work or to resume daily activities earlier with various times of PAR following IHR. The trial will assess feasibility and safety of delivering this postoperative recommendation, and if successful, will progress to an implementation into the daily routine following IHR as a new guideline.

### 4.1. Strengths and limitations

Compared to other studies, this study aims to include a small prospective patient cohort (n = 90) and focuses solely on patients with IHR in sublay technique. This study has a multicenter design, which increase generalizability. The way this intervention is set-up makes it feasible to implement it in other settings as well.

## 5. Availability of data and materials

All data will be kept secure and confidential following institution rules for data storage and will be available to all contributors of this protocol. Dissemination of results will be carried out through publication of scientific articles in peer-reviewed journals.

## 6. Ethic's approval and consent to participate

The study was approved by the Ethics Committee of the University hospital Magdeburg (04-27-2020, ID 46/20), Germany. Informed consent will be obtained from eligible patients before

screening by a member of the research or clinical team. The results of this study will be presented with interest in the management of postoperative care after incisional hernia repair with the focus on a shortened recovery time. The results of this trial will be presented to international conference with interest in hernia surgery and published in a peer-reviewed journal.

## 7. Consent

Studies on patients or volunteers require ethics committee approval and fully informed written consent which should be documented in the paper.

Authors must obtain written and signed consent to publish a case report from the patient (or, where applicable, the patient's guardian or next of kin) prior to submission. We ask Authors to confirm as part of the submission process that such consent has been obtained, and the manuscript must include a statement to this effect in a consent section at the end of the manuscript, as follows: "Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request".

Patients have a right to privacy. Patients' and volunteers' names, initials, or hospital numbers should not be used. Images of patients or volunteers should not be used unless the information is essential for scientific purposes and explicit permission has been given as part of the consent. If such consent is made subject to any conditions, the Editor in Chief must be made aware of all such conditions.

Even where consent has been given, identifying details should be omitted if they are not essential. If identifying characteristics are altered to protect anonymity, such as in genetic pedigrees, authors should provide assurance that alterations do not distort scientific meaning and editors should so note.

## 8. Guarantor

The Guarantor is the one or more people who accept full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish

## 9. Registration of Research Studies

In accordance with the Declaration of Helsinki 2013, all research involving human participants has to be registered in a publicly accessible database. Please enter the name of the registry and the unique identifying number (UIN) of your study.

You can register any type of research at <http://www.researchregistry.com> to obtain your UIN if you have not already registered. This is mandatory for human studies only. Trials and

certain observational research can also be registered elsewhere such as: [ClinicalTrials.gov](https://www.clinicaltrials.gov) or ISRCTN or numerous other registries.

## Author contribution

Please specify the contribution of each author to the paper, e.g. study concept or design, data collection, data analysis or interpretation, writing the paper, others, who have contributed in other ways, should be listed as contributors.

## Declaration of Competing Interest

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.

## References

- [1] J. Hoer et al., Factors influencing the development of incisional hernia. A retrospective study of 2,983 laparotomy patients over a period of 10 years, *Chirurg* 73 (5) (2002) 474–480.
- [2] J.W. Burger et al., Long-term follow-up of a randomized controlled trial of suture versus mesh repair of incisional hernia, *Ann. Surg.* 240 (4) (2004) 578–583, discussion 583–5.
- [3] R. Bittner et al., Guidelines for laparoscopic treatment of ventral and incisional abdominal wall hernias (International Endohernia Society [IEHS])-Part III, *Surg. Endosc.* 28 (2) (2014) 380–404.
- [4] R. Bittner et al., Guidelines for laparoscopic treatment of ventral and incisional abdominal wall hernias (International Endohernia Society [IEHS])-part 1, *Surg. Endosc.* 28 (1) (2014) 2–29.
- [5] R. Bittner et al., Guidelines for laparoscopic treatment of ventral and incisional abdominal wall hernias (International Endohernia Society [IEHS])-Part 2, *Surg. Endosc.* 28 (2) (2014) 353–379.
- [6] R. Bittner et al., Update of Guidelines for laparoscopic treatment of ventral and incisional abdominal wall hernias (International Endohernia Society [IEHS]): part B, *Surg. Endosc.* (2019).
- [7] J.L. Holihan et al., Mesh location in open ventral hernia repair: a systematic review and network meta-analysis, *World J. Surg.* 40 (1) (2016) 89–99.
- [8] Obermaier R., P.F., Ulrich T., *Hernienchirurgie*. 2009.
- [9] C. Paasch, S. Anders, M.W. Strik, Postoperative-treatment following open incisional hernia repair: a survey and a review of literature, *Int. J. Surg.* 53 (2018) 320–325.
- [10] C. Paasch et al., Patient reported outcome following incisional hernia repair: a survey on 163 patients at two maximum care hospitals, *Ann. Med. Surg. (Lond.)* 44 (2019) 5–12.
- [11] D. Dindo, N. Demartines, P.A. Clavien, Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey, *Ann. Surg.* 240 (2) (2004) 205–213.
- [12] E. Bassini, Ueber die behandlung des Leistenbruches, *Arch klin Chir* 40 (1890) 429–476.
- [13] E.W. Taylor, E.P. Dewar, Early return to work after repair of a unilateral inguinal hernia, *Br. J. Surg.* 70 (10) (1983) 599–600.
- [14] S. Majercik, V. Tsikitis, D.A. Iannitti, Strength of tissue attachment to mesh after ventral hernia repair with synthetic composite mesh in a porcine model, *Surg. Endosc.* 20 (11) (2006) 1671–1674.
- [15] A.C. Vailas et al., Physical activity and its influence on the repair process of medial collateral ligaments, *Connect Tissue Res.* 9 (1) (1981) 25–31.
- [16] S. Olmi et al., Laparoscopic versus open incisional hernia repair: an open randomized controlled study, *Surg. Endosc.* 21 (4) (2007) 555–559.