Author’s response to reviews

Title: Transabdominal laparoscopic retroperitoneal neurectomy for chronic pain after inguinal hernia repair and appendicectomy - a matched-pair study.

Authors:
Ioannis Karampinis (jkarabinis@yahoo.com)
Johannes Weiss (johannes.weiss@grn.de)
Lothar Pilz (lothar.pilz@medma.uni-heidelberg.de)
Stefan Post (stefan.post@umm.de)
Florian Herrle (florian.herrle@umm.de)

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Author’s response to reviews:
Reviewer #1: I commend the authors for pursuing this research and treating this challenging condition. I am interested in their approach and clinical success with this operative treatment. I have a few reservations and comments on the design of the study and the surgical approach.

From a surgical perspective, I have some reservation about the choice of neurectomy. All 9 patients underwent neurectomy of the lateral femoral cutaneous nerve but only one patient (that had undergone TEP repair) had any potential mechanism for injury of this nerve. The LFCN exits below and lateral to the the inguinal ligament and is not at risk in any anterior repair. Sacrifice will lead to greater sensory disturbance and an increased risk of deafferentation hypersensitivitiy. This nerve is typically sacrificed only sparingly. The study really follows the clinical effect of neurectomy of the GFN and its branches as only 3 patients had the ilioinguinal nerve resected. In general, this is the most common nerve injured from an anterior inguinal repair of open operation. Dermatomal mapping may help to guide preoperative planning in the future and increase efficicy rates for selective neurectomy and decrease unnecessary collateral numbness.
As a point of advice, we have performed over 1000 neurectomies and 100 lap retroperitoneal and from this experience we are quite selective on which patients benefit from retroperitoneal surgery. The numbness in much greater and the accompanying abdominal wall laxity from motor denervation make this technique best suited for those with failed prior neurectomy and prior posterior repair where nerve injury is proximal to the transversalis fascia. In these patients, the surgery is very effective when selected for neuropathic pain.

As a study in operative technique, this small series of 9 patients is in line with other reports of selective neurectomy with efficacy rates typically in the 60-70 percent range. The results are reasonable and the technique safe. I am appreciative of the effort and work involved with assessing QOL especially at long term follow up. The matched pair analysis doesn't significantly contribute to this analysis as the QOL of the neurectomy group will always be lower than the control group as this cohort has severe pain which is why they come for intervention. This decline in QOL is not a function of the remedial operation but of their underlying inguinodynia. The corresponding control group would be inguinodynia with medical management or inguinodynia with open neurectomy. This would better characterize the effect of your intervention and likely demonstrate either equivalence of the intervention of improvement. In its current state, the matching to normal post-op controls confounds the findings and conclusions.

Revision according to the 1st reviewer's comments:

The laparoscopic retroperitoneal neurectomy was introduced in our department in March 2010. As guide for the neurectomy and the nerves damaged we used the clinical examination and the localization of the pain. The first 3 patients we operated using this technique complained of pain in the proximal thigh and genital region so we decided to resect the LFCN and GFN. Those patients were readministered for clinical follow up during the early postoperative period and described a significant improvement in their pain status. We did not experience significant postoperative morbidity since 2 of those patients had a hypoesthesia of the neurectomied region, a predictable complication of the neurectomy, and one did not report hypoesthesia. This fact encouraged us in performing the neurectomy including the LFCN.
Here we should mention that at this period the 2011-guideline for prevention and management of postoperative chronic pain had not been published yet and the available literature regarding the nerve selection for neurectomy was confusing since there were trials supporting the neurectomy of the LFCN (Bower Am Surg 1996, Kraehenbuehl Br J Surg 1997, Aasvang (Review) Br J Surg 2005, Hakeem WJGS 2011. At the time of the publication of the above mentioned guideline we had operated 7 of 9 patients and had acceptable results, comparable with other cohort studies and low morbidity, mainly postoperative hypoesthesia. Furthermore, the guidelines did not discuss in detail which nerves should be included in the neurectomy. The neurectomy of the LFCN was extensively discussed in the presentation of our study in the abdominal wall surgery congress in 2015 in Milano. The available data are pretty much clear now that the LFCN should not be primarily included in the neurectomy and this fact has been implemented in our surgical practice.

Concerning the QoL data, it is clear that analyzing the quality of life in patients with chronic pain we expected to find markedly lower values compared to patients without chronic pain. The idea of conducting this data-analysis evolved during the clinical examination of a patient who had been previously operated for a hernia and was admitted to our clinic because of an acute cholecystitis. As I asked him if he had any complaints regarding the hernia-operation he answered that the operation had made his symptoms much worse. This patient had never searched for medical help for this problem. On this basis we decided to ask more patients. We had initially planned a 1:3 matching ratio but it was very difficult to find controls with a Lotheissen operation 25 years ago so we reduced the patient-control ratio to 1:1. In the overall analysis we found that the pain status of the ‘healthy population ‘concerning the hernia operation was not negligible since there was a relevant amount of patients with pain who were not referred to adequate therapy. Furthermore, the SF-36 questionnaire had never been used for this reason before and no valid data concerning the actual disability of those patients existed so we were interested to see the data in comparison to published values of other painful diseases.

We fully agree with your point, that the best control group would have been an inguinodynia-population treated with medication or intervention/infiltrations or even with an open neurectomy. We have added this consideration in the discussion section (page13, limitations paragraph, highlighted). In our setting the formation of such a control group would have been virtually unfeasible as we do not dispose of such a large population of patients treated for chronic inguinodynia with different modalities.
Reviewer #2: What evidence is there that chronic pain is related to nerve damage. The authors do not give a clear description of how they found the ilioinguinal or iliohypogastric nerves and how they determined what nerves they planned to excise. One patient in the control group had severe pain yet the pain score was 0, can they please explain?

Revision according to the 2nd reviewer's comments:

There are several studies which have addressed the problem of postherniorrhaphy chronic pain. The innervation of the groin and the anatomical localization of the four nerves may lead to intraoperative damage of the ilioinguinal, iliohypogastric, genitofemoral and lateral femoral cutaneous nerve. (Kehlet, Hernia 2002, Rab, Plastic and Reconstructive Surgery 2001, Amid, Hernia 2004, Hakeem, World J Gastrointest Surg 2011). To the best of our knowledge no special test exists at the moment which can give a reliable answer if a direct nerve damage has occurred. Additionally, there is not a valid diagnostic algorithm on how to diagnose a neuropathic from a not neuropathic pain. Many surgeons perform preoperative infiltrations and based on the result of those decide if a neurectomy is indicated, others try a medical treatment and if this fails perform the neurectomy. According to the available literature, a neurectomy following a failed medical treatment and based on a careful patient selection can offer pain relief in 60-90% of the cases. The decision which nerves to resect was based on the clinical examination and the symptoms of the patient. Most of our patients described pain in the genital region and the upper thigh and fewer patients had pain directly in the incision area. According to the preoperative clinical examination the operating surgeon decided the extent of the neurectomy. The iliohypogastric and ilioinguinal nerves were localized and resected after penetrating the psoas muscle, 2-3 cm laterally, as they travel on the quadratus lumborum muscle to the lateral abdominal wall. The 12th rib and the thoracic-lumbar spine were used for the intraoperative orientation. Further caudal and lateral of the ilioinguinal nerve we localized the long lateral femoral cutaneous nerve and medially and caudally of the LFCN the genitofemoral nerve with it’s branches (pages 6 and 7, Technical description of transabdominal laparoscopic retroperitoneal neurectomy, highlighted).
Concerning the severe pain status of the control patient and the pain score of 0 we would like to point out that the severe pain is referred to the status before the primary operation, in this case before the appendicectomy. The patient described severe pain because of the acute appendicitis. The score of 0 is referred to the pain status of the postoperative period which was, in this case, 0.