

ORIGINAL ARTICLE

Functional abdominal complaints occurred frequently in living liver donors after donation

KARL SØNDENAA¹, GABRIEL E. GONDOLESI², SASAN ROAYAIE², JODY S. GOLDMAN², TRYGVE HAUSKEN³ & MYRON E. SCHWARTZ²

¹Department of Surgical Sciences, University of Bergen, Norway, ²Adult Liver Transplantation & Hepatobiliary Surgery, Mount Sinai School of Medicine and Recanati/Miller Transplantation Institute, Mount Sinai Medical Center, New York, USA, and ³Institute of Medicine, University of Bergen, Bergen, Norway

Abstract

Background. Donor outcome after living donor liver transplantation has not been examined extensively with regard to postoperative abdominal complaints. We wanted to examine the extent and type of abdominal complaints after removal of a part of the liver and gallbladder in living donors as well as potential similarities with known disorders. **Methods.** Twelve patients of mixed ethnicity, nine men, aged 18–45 years, and three women, aged 32–46 years, were enrolled in the study during a 3-year period and followed up at 6 and 12 months. Patients filled out questionnaires pertaining to functional abdominal complaints (FAC) using a recognized questionnaire, Rome II, as well as specific abdominal pain symptoms known from gallstone disease. **Results.** FAC occurred in 11 patients at 6 months and nine patients at 12 months while abdominal pain occurred in seven and six patients, respectively. Three patients had FAC but no abdominal pain while two patients had no complaints at 12 months. Irritable bowel syndrome (IBS) was found in the majority of patients. **Conclusions.** FAC and pain seemed to indicate a general postoperative disorder, of a psychosomatic character, and not connected with removal of part of the liver and gallbladder in particular. However, the occurrence of IBS and FD should merit attention, as they are known to impair quality of life.

Key Words: Abdominal postoperative pain, cholecystectomy, functional dyspepsia, living liver donor, liver resection, liver transplantation

Introduction

Living liver donation has emerged in recent times as an acceptable method of treating advanced liver disease. However, it has been shown to cause a diversity of consequences for the donor [1]. Reports have focused on the more dramatic consequences represented by postoperative morbidity [2–4] as well as psychosomatic disorders [5–13].

In living adult liver donation, it has become customary to remove the right hemiliver from the donor because of the volume needed for sufficient liver function in the recipient. Consequently the gallbladder is also removed. However, it is largely unknown if removal of the gallbladder with part of the liver in

healthy individuals will lead to any specific abdominal symptoms, like post-cholecystectomy pain. In symptomatic gallstone patients, such symptoms have been observed in 27% of patients after cholecystectomy [14]. Psychosomatic predisposition has been vindicated in the origin of post-cholecystectomy symptoms [15].

Functional abdominal complaints (FAC) such as gastro-esophageal reflux disease (GERD) symptoms, functional dyspepsia (FD), and irritable bowel syndrome (IBS), which are common in the population, seem to coexist or share similar pathological pathways with symptomatic gallstone disease. One study found an 11% incidence of postoperative dyspepsia in living liver donors [16], although as many as 71% with mild

symptoms, mainly abdominal, have been reported [13] but FAC per se have not been properly examined under these circumstances and psychosomatic complaints in general are inconsistently reported [1].

The aim of the present pilot study was to examine FAC in donors after living adult liver donation with a secondary focus on pain characteristics.

Material and methods

Study population and design

Because of the particular circumstances associated with living donor transplantation versus cadaveric transplantation, the patients were recruited over a fairly long stretch of time, from March 2004 to July 2006.

Inclusion and exclusion criteria

Consecutive persons between 18 and 60 years of age and with no gallbladder stones demonstrated at imaging work-up who had the right hemiliver (right liver lobe) removed, gallbladder inclusive, were included. Patients with gallbladder stones demonstrated pre- or per-operatively or unwillingness to participate were exclusion criteria. Donation in case of acute liver failure incurred too much organizing stress on the transplant team and the donor to be able to enroll study candidates in a relaxed and orderly fashion.

Investigational methods – questionnaires

FAC, as GERD, FD, and IBS, were assessed using the Rome II criteria using the patient filled out questionnaire. This questionnaire also has questions dealing with abdominal pain presumably caused by gallstone disease. Chronic symptoms are defined in Rome II as being present for the last 3 months.

The donor patient also filled out a self-made pain questionnaire (SMQ). Symptoms accredited to gallstone disease were previously collected in connection with interviews of several hundred gallstone patients. Thus, it should theoretically complement the Rome II questionnaire in an attempt to characterize the pain symptoms more accurately. The frequency of pain attacks was recorded to say something about pain severity. The SMQ sought to characterize pain by asking for information about location of pain, area of strongest pain, pain pattern, referred pain, urge to move around, duration of pain episodes, time of appearance during the day, nausea, and use of pain medication. Scoring pain severity on a Visual Analog Scale (VAS) was requested.

CT and MRI of the liver, gallbladder, and common bile duct were routinely done. Removed gallbladders underwent routine histological examination.

Follow-up

Patients were seen at the clinic 6 and 12 months after the operation. The preoperative forms were then repeated.

Ethics committee

The Internal Review Board at Mount Sinai Medical Center approved the study (IRB #:03-1202 SU).

Statistics

Exact McNemar's test for two related binomial proportions, Cytel Studio v. 8 statistical package was used to analyze changes in functional abdominal complaints from the pre-operative situation to 6 and 12 months post-operative.

Results

Only 12 patients referred for live liver donor operations were enrolled in the study because of a more favorable waiting list policy for the recipients in this group during the study period. There were nine men, mean age 32 years, range 18–45 years, and three women, aged 32, 35, and 46 years. Ethnicity was mixed with patients of Caucasian (n = 7; men = 4), Hispanic (3 men), Asian (one man), and Afro-American (one man) origin. One patient (#6) refused follow-up at 12 months.

Functional abdominal complaints (FAC) and pain

FAC appeared post-operatively in all patients at one point at the two clinic visits. According to the Rome II classification, IBS was found in most patients and FD was observed in about half of the patients (see Table I).

As shown in Table I, one patient had FAC and abdominal pain before the operation. The symptoms and pain persisted at follow-up. Two other patients reported preoperative dyspepsia without pain and had variable FAC during 1 year of follow-up.

After 1 year, two patients had neither FAC nor pain while three patients had FAC without pain.

Abdominal pain characteristics

Abdominal pain occurred in seven patients at 6 months and in six patients at 12 months (see

Table I. Presence of pain and classification of functional abdominal complaints (FAC) according to the Rome II questionnaire in 12 living liver donors.

| Variable | No of patients (patient #) | | |
|-------------------|----------------------------|---------------------|------------------|
| | Preoperative | 6 months* | 12 months** |
| Dyspepsia | 3 (4,9,10) | 5 (4,6,7,9,12) | 6 (1,2,4,7,8,12) |
| IBS | 1 (4) | 9 (2-8,10,11) | 8 (1-5,7,8,10) |
| Abdominal pain | 1 (4) | 7 (1,2,4,6,7,10,12) | 6 (1,3-5,7,12) |
| FAC and pain | 1 | 6 | 6 |
| No. of complaints | 9 | 0 | 2 |

Recipients of graft #8 and #10 died, #7 had a ventral hernia repair.
 *Patient #1 did not return Rome II questionnaire.
 **Patient #6 absent at 12 months.

Table II). Thus, five patients (of 11) reported no abdominal pain at 1 year. A pain attack pattern only vaguely similar to typical gallstone pain was found in two patients at 6 months and one at 12 (patients #6 and #10 and #7, respectively). The last one used pain medication.

Complications

Patient number 7 had a ventral hernia repair more than 2 years after donation. The recipients of graft numbers 8 and 10 passed away within 30 days postoperative.

Statistics

There was a significant increase in FAC in the post-operative setting ($p = 0.004$; OR = infinity; 95% CI: 2.34 to infinity).

Discussion

It is customary to remove the right liver lobe (hemiliver) in living donor adult liver donation because of the greater volume needed for the graft to function optimally in the recipient [2,3]. The gallbladder is also removed because it is situated on the partition line in the liver. It has for many years been thought that removal of a part of the liver and a normal gallbladder does not have any consequences for the individual concerned. However, post-cholecystectomy symptoms, mainly pain, have been a recognized condition in gallstone disease albeit without the cause being well proven or properly defined [14,17]. One study found more psychosomatic disturbances in patients that complained of post-cholecystectomy symptoms [15]. It was our intention to investigate abdominal complaints in liver donors using known disease patterns for comparison [18].

FAC consists of two main subgroups, functional dyspepsia (FD) and irritable bowel syndrome (IBS), with overlapping features making them both symptomatic of an irritable gut [19]. Prevalence of FAC is between 10% and 20% around the world [20,21]. In the West, there tends to be a female predominance. IBS commonly begins before the age of 35 in about 50% of people, but may occur at any age. A formal definition of FAC is given by the Rome II criteria [22] although this is mostly a research tool that uses several levels of symptoms present at various lengths of time. More recently, Rome III has been introduced. It has been found that Rome II may over-score symptoms compared with complaints diagnosed by general practitioners [23]. It is therefore a point of concern whether a self-assessment questionnaire like the Rome II will make the patient report more complaints

Table II. Occurrence and characteristics of pre-operative and post-operative abdominal pain in 12 living liver donors.

| Variable | Preoperative | 6 months* (patient no.) | 12 months** |
|--|--------------|-------------------------|----------------|
| Abdominal pain | 1 (4) | 7 (1,2,4,6,7,10,12) | 6 (1,3-5,7,12) |
| Pain attacks | 1 (4) | 5 (1,2,4,6,10) | 4 (3-5,7) |
| Chronic pain | 1 (4) | 2 (4,7) | 4 (1,4,7,12) |
| Dominant in RUQ | 0 | 4 (1,4,7,10) | 3 (1,7,12) |
| Dominant in lower abdomen | 1 (4) | 2 (2,12) | 3 (3-5) |
| Pain pattern A or B | 1 (4) | 2 (6,12) | 3 (4,7,12) |
| Urge to move around | 0 | 1 (6) | 1 (12) |
| Duration of attacks >30 min | 1 (4) | 3 (6,10,12) | 1 (12) |
| Frequency of pain attacks, mean (range) per 3 months | 20 | 5.4 (1-10) | 6.4 (2-12) |
| Pain strength on VAS, mean (range) | 60 | 66 (22-81) | 54 (22-76) |
| Pain medication | 0 | 1 (12) | 3 (5,7,12) |

Abbreviation: RUQ = subcostal or epigastric area.
 Pain pattern A and B.
 Recipients of graft #8 and #10 died, #7 had a ventral hernia repair.
 *Patient #1 did not return Rome II questionnaire.
 **Patient #6 absent at 12 month.

than will be revealed by a professional interview [11]. We did not evaluate this assumption further.

Our results showed that three patients had some complaints preoperatively, consistent with that of the general population. Post-operative, abdominal complaints occurred in all patients at 6 months. Six patients had FAC and pain whereas five patients had FAC without pain. One patient had only pain. At 12 months, six patients had FAC and pain whereas three patients had FAC without pain. Two patients did not report any abdominal complaints. The majority suffered from IBS at both occasions.

Minor abdominal pain was present in one patient before the operation and this pain continued post-operatively. Pain medication was not used. Post-operative, five and four patients had what they perceived as pain attacks, and one and two additional patients described chronic pain at the 6 and 12 months follow-ups. One patient who had a ventral hernia repair had a mix of the two. One and three patients used pain medication at each follow-up. Abdominal pain did not seem to improve with time as judged by the number of patients with pain but judged by a mean VAS reading of 66 versus 54, there was a slight improvement in pain strength.

Two patients had predominantly upper abdominal pain symptoms at the 6 months (one on the left side) and one patient at the 1-year mark. The last one used pain medication. All three had FAC. Because of a stringent lack of definition in gallstone disease, any complaint of dyspepsia and abdominal pain after cholecystectomy might be classified as post-cholecystectomy symptoms. One study found that after cholecystectomy pain was present in 27%, 18% diffuse and 9% pain attacks resembling the preoperative condition [14]. The observations of pain in our patients were inconsistent because scoring by using the SMQ did not obtain the kind of result that patients without proper alleviation experience after cholecystectomy. The association with FAC dominated similar to what can be seen in post-cholecystectomy conditions. Consequently, we were not able to detect any obvious connection between pain expression and removal of the gallbladder, although such a connection could not be ruled out entirely given the complex clinical picture often seen in gallstone patients. The VAS score was intermediate between that seen in gallstone patients before (mean 80) and after (mean 30) cholecystectomy [14].

Findings of pain and abdominal or psychosomatic complaints by others in living liver donors have been contentious. Two German studies, using much the same group of patients but different measurement tools, found that 26% of donors had limb pain and fatigue or tiredness at 6 months whereas 11% showed

a stress reaction [7,12]. With some limitations, a review [1], found a morbidity rate of 31% dominated by abdominal discomfort. As many as 71% have had abdominal symptoms [13]. An American study [16] reported postoperative pain in 37% and gastric dysfunction and dyspepsia in 11%. It is conceivable that several dysfunctions may have caused these impairments such as reported gastric stasis from nerve injury or adhesions, wound hernia or simply wound pain or cosmetic concern with the wound and last but not least, a impaired psychic function causing reduced quality of life. Laparotomy as a cause of symptoms is debatable. The patient with hernia had pain as well as FD and IBS. Post-laparotomy pain may occur in 22% of patients after cholecystectomy [14]. In that particular study, more than two-thirds had undergone laparoscopic surgery [14]. In general, those with the most severe preoperative complaints are more likely to suffer from post-operative pain [14,18,24]. This indicates that our patients acquired post-operative symptoms related to their post-surgical condition. Pain related to the abdominal incision could not entirely be ruled out although post-operative pain after the laparoscopic and open approach in gallstone patients has not been different [14].

Our study population consisted of a majority of men and had a diverse ethnic background. These circumstances may well have influenced the result. However, studies of FAC have not shown great ethnic differences [20,21]. Living donors may subject to a great deal of psychological stress. Two of our donors lost their recipients shortly after the donation. These two patients both had IBS at 6 and 12 months but only one of them mentioned pain at 6 months. Adverse outcome for the recipient has been mentioned as a negative influence on the donor [3,6], although not observed by others [11]. Complications after the donor operation have affected the psychosocial status of the donor [11] but again not observed by others [7,8]. One patient who had a ventral hernia repair had both FAC and pain. A Japanese study [8] found more psychiatric disease after donation. A tendency for the donors to use more analgesics than the recipient has been observed in Japanese patients.

It has been advocated that all donors should be followed up for a minimum of 1 year after donation to avoid missing consequences of both somatic and psychosomatic disease [16]. Many donors or programs fail to achieve this for various reasons [1,4]. Patients with IBS who attend hospital clinics may have poorer quality of life than those with chronic diseases [25]. Quality of life in donors was found to be severely impaired in 14%, at least temporarily [11]. Under such circumstances, it is conceivable that the

stress of donation elicited FD and IBS in our patients. However, we did not do any psychometric testing in our patients.

We conclude that the post-operative symptoms of the living donor liver donation seems to be dominated by FAC, usually accompanied by pain, and almost all patients suffered from this at 6 months with slight improvement at 1 year. We could not conclude in this preliminary study that pain was caused by organ removal per se because of the lack of a control group, but this issue might be targeted in a larger patient sample such as in a multicenter study and possibly compared with patients undergoing hemihepatectomy as a reference group. In light of the life-threatening situation for the recipient living liver donation should still be an option in the transplant surgeon's armamentarium but donors need counseling and close follow-up for a considerable time.

Acknowledgements

The authors are grateful to Dr. J. A. Dumot of the Cleveland Clinic, for assistance in translating the SMQ and to statistician Geir Egil Eide, PhD, for doing the statistical analysis.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

- [1] Beavers KL, Sandler RS, Shrestha R. Donor morbidity associated with right lobectomy for living donor liver transplantation to adult recipients: A systematic review. *Liver Transpl* 2002;8:110–7.
- [2] Umeshita K, Fujiwara K, Kiyosawa K, Makuuchi M, Satomi S, Sugimachi K, et al. Operative morbidity of living donors in Japan. *Lancet* 2003;362:687–90.
- [3] Shah SA, Grant DR, Greig PD, McGilvray ID, Adcock LD, Girgrah N, et al. Analysis and outcomes of right lobe hepatectomy in 101 consecutive living donors. *Am J Transplant* 2005;5:2764–9.
- [4] Rudow DL, Brown RS Jr, Emond JC, Marratta D, Bellemare S, Kinkhabwala M. One-year morbidity after donor right hepatectomy. *Liver Transpl* 2004;10:1428–31.
- [5] Fukunishi I, Sugawara Y, Makuuchi M, Surman O. Pain in liver donors. *Psychosomatics* 2003;44:172–3.
- [6] Kim-Schluger L, Florman SS, Schiano T, O'Rourke M, Gagliardi R, Drooker M, et al. Quality of life for adult liver transplantation. *Transplantation* 2002;73:1593–7.
- [7] Walter M, Bronner E, Pascher A, Steinmuller T, Neuhaus P, Klapp BF, Danzer G. Psychosocial outcome of living donors after living donor liver transplantation: a pilot study. *Clin Transplant* 2002;16:339–44.
- [8] Kita Y, Fukunishi I, Harihara Y, Hirata M, Kubota K, Takayama T, Kawarasaki H, et al. Psychiatric disorders in living-related liver transplantation. *Transplant Proc* 2001;33:1350–1.
- [9] Diaz GC, Renz JF, Mudge C, Roberts JP, Ascher NL, Emond JC, Rosenthal P. Donor health assessment after living-donor liver transplantation. *Ann Surg* 2002;236:120–6.
- [10] Trotter JF, Hill-Callahan MH, Gillespie BW, Nielsen CA, Saab S, Shrestha R, Talamantes MM, et al. Severe psychiatric problems in right hepatic lobe donors for living donor liver transplantation. *Transplantation* 2007;83:1506–8.
- [11] Erim Y, Beckmann M, Valentin-Gamazo C, Malago M, Frilling A, Schlaak JF, et al. Quality of life and psychiatric complications after adult living donor liver transplantation. *Liver Transpl* 2006;12:1782–90.
- [12] Walter M, Papachristou C, Fliege H, Hildebrandt M, Pascher A, Steinmuller T, et al. Psychosocial stress of living donors after living donor liver transplantation. *Transplant Proc* 2002;34:3291–2.
- [13] Trotter JF, Talamantes M, McClure M, McClure M, Wachs M, Bak T, et al. Right hepatic lobe donation for living donor liver transplantation: impact on donor quality of life. *Liver Transpl* 2001;7:485–93.
- [14] Vetthus M, Berhane T, Søreide O, Søndena K. Pain persists in many patients five years after removal of the gallbladder. Observations from two randomized controlled trials of symptomatic, noncomplicated gallstone disease and acute cholecystitis. *J Gastrointest Surg* 2005;9:826–31.
- [15] Stefaniak T, Vingerhoets A, Babinska D, Trus M, Glowacki J, Dymecki D, et al. Psychological factors influencing results of cholecystectomy. *Scand J Gastroenterol* 2004;39:127–32.
- [16] Renz JF, Roberts JP. Long-term complications of living donor liver transplantation. *Liver Transpl* 2000;6 (Suppl 2): S73–6.
- [17] Haldestam I, Kullman E, Borch K. Defined indications for elective cholecystectomy for gallstone disease. *Br J Surg* 2008;95:620–6.
- [18] Berhane T, Hausken T, Olafsson S, Vetthus M, Søndena K. Pain attacks in gallstone disease have a characteristic pattern and are commonly accompanied by dyspepsia. *Scand J Gastroenterol* 2006;41:93–101.
- [19] Choung RS, Locke III GR, Schleck CD, Zinsmeister AR, Talley NJ. Do distinct dyspepsia subgroups exist in the community? A population-based study. *Am J Gastroenterol* 2007;102:1983–9.
- [20] Camellieri M, Choi MG. Review article: irritable bowel syndrome. *Aliment Pharmacol Ther* 1997;11:3–15.
- [21] Locke GR 3rd, Zinsmeister AR, Fett SL, Melton LJ 3rd, Talley NJ. Overlap of gastrointestinal symptom complexes in a US community. *Neurogastroenterol Motil* 2005;17:29–34.
- [22] Drossman DA, Corazziari E, Talley NJ, Thompson WG, Whitehead WE. Rome II: a multinational consensus document on functional gastrointestinal disorders. *Gut* 1999;45:1–81.
- [23] Vandvik PO, Aabakken L, Farup PG. Diagnosing irritable bowel syndrome: poor agreement between general practitioners and the Rome II criteria. *Scand J Gastroenterol* 2004;39:448–53.
- [24] Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. *Lancet* 2006;367:1618–25.
- [25] Pace F, Molteni P, Bollani S, Sarzi-Puttini, Stockbrügger R, Porro GB, Drossman DA. Inflammatory bowel disease versus irritable bowel syndrome: a hospital-based, case-control study of disease impact on quality of life. *Scand J Gastroenterol* 2003;38:1031–8.

Copyright of Scandinavian Journal of Gastroenterology is the property of Taylor & Francis Ltd and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.