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Increased risk of ventral hernia recurrence after pregnancy: A nationwide register-based study

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ABSTRACT

Background: Female patients of reproductive age constitute a substantial portion of patients undergoing ventral hernia repair, however the impact of pregnancy on the risk of recurrence is scarcely documented. The aim of the study was to evaluate if pregnancy following ventral hernia repair was associated with an increased risk of recurrence.

Methods: This nationwide cohort study included all female patients of reproductive age registered in the Danish Ventral Hernia Database with ventral hernia repair between 2007 and 2013. The primary outcome was ventral hernia recurrence. Multivariable extended Cox regression analysis was performed.

Results: A total of 3578 patients were included in the study, 267 (7.5%) of whom subsequently became pregnant during follow-up. The median follow-up was 3.1 years (range 0–8.4 years). Pregnancy was independently associated with recurrence (hazard ratio 1.56, 95% confidence interval 1.09–2.25, $P = 0.016$).

Conclusions: Pregnancy after ventral hernia repair was independently associated with ventral hernia recurrence.

1. Introduction

Ventral hernia repair is one of the most commonly performed general surgical procedures.[1] Despite advances in surgical technique, the risk of recurrence remains high, up to 8% after umbilical or epigastric hernia repair and 37% after incisional hernia repair.[2] Risk factors for recurrence include suture repair, surgical site infection, larger hernia defect size, high body mass index, young age and smoking.[3–6]

Although women of reproductive age constitute a substantial portion of patients with ventral hernia, consensus lacks on the timing of surgical repair for patients who subsequently might become pregnant.[2,7,8] Few studies have reported on the ventral hernia recurrence rate following pregnancy. Two case series concluded that reluctance towards pre-pregnancy repair is probably unjustified, while a cohort study found that pregnancy was associated with reoperation for recurrence.[9–11] An untreated hernia may expand and become increasingly symptomatic during pregnancy, potentially leading to emergency repair. However, pregnancy associated raised intraabdominal pressure and increased abdominal wall tension might lead to recurrence.[12,13]

On this background we hypothesized that pregnancy results in an increased risk of ventral hernia recurrence. The aim of this nationwide, register-based study on ventral hernia repairs was to examine if subsequent pregnancy was associated with hernia recurrence.

2. Materials and methods

This was a retrospective nationwide cohort study based on prospectively registered data. The reporting of this study conforms to the STROBE statement.[14]

The study cohort was established from a search in the Danish Ventral Hernia Database, which holds both peri- and postoperative information on patients undergoing ventral hernia repair in Denmark.[15] The operating surgeon is obliged by law to register in the database through an online registration form immediately after

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completion of the procedure. All female patients of reproductive age who underwent ventral hernia repair (umbilical, epigastric or incisional) between 1st of January 2007 and 8th of April 2013 were identified and included. The patients were defined as reproductive if their age was between 12 and 45 years at the day of index repair.[16,17] The first registered ventral hernia repair was defined as the index repair. Obstetric history for each patient was available until 31st of December 2013 and was retrieved from the Danish Medical Birth Registry which holds data on all births, including home deliveries.[18] To estimate the time-dependent risk associated with subsequent pregnancy, the date of the first delivery subsequent to index surgery was recorded. To estimate the pregnancy initiation date, the pregnancy period was defined as 267 days preceding the delivery.[19] Patients who were pregnant at the time of index repair were excluded.

The primary outcome of the study was ventral hernia recurrence. This was defined as diagnosis of recurrence or reoperation for recurrence, according to registration in the Danish National Patient Registry (DNPR) which holds data on all in- and outpatient diagnoses and procedures from both public and private hospitals in Denmark.[20] DNPR makes use of the 10th revision of the International Classification of Diseases (ICD-10) and the common Nordic NOMESCO Classification of Surgical Procedures.[21,22] Several studies have validated the DNPR for general surgical diseases, finding an overall positive predictive value of 89% for correct diagnoses.[23] In Denmark, consensus is to establish the diagnosis of clinical recurrence based on physical examination alone, supplemented with radiologic examination or ultrasonography in case of doubt. Follow-up data was available until 20 May 2015, however as obstetric history was only available until 31 December 2013, the follow-up ended at this date if a delivery was not yet noted. The Danish Civil Registration System provided date of death or emigration. All registries were linked at an individual level through the Danish civil registration number, which is unique to each individual.[24]

To identify potential confounders and effect modifiers, the following variables were included from the Danish Ventral Hernia Database: age, hernia defect size, hernia type, mesh/suture repair, surgical approach and priority of the procedure (emergency or elective). The formula for an ellipse, π x (maximal horizontal diameter/2) x (maximal vertical diameter/2), was used to calculate the area of the hernia defect. In cases where the surgeon repaired more than one defect, the measured dimensions were added together.

The patients were followed from the day of index repair until diagnosis of recurrence, reoperation, emigration, death or end of follow up. Univariable analyses comparing patients with and without subsequent pregnancy were performed with Mann Whitney *U* test for continuous variables as none were normally distributed. Categorical variables were analyzed with Pearson's Chi-squared test or Fisher's exact test where appropriate.

Extended Cox regression analyses were performed with right censoring at times of emigration, death or end of follow-up in order to account for varying duration of follow-up. Subsequent pregnancy was modelled as a time-dependent variable.[25] Pregnancy is associated with an obligatory recurrence-free time interval from index repair until pregnancy, because recurrence prior to conception would be considered unexposed to pregnancy. A conventional time-fixed model incorrectly projects back the time of pregnancy to baseline and ignores the obligatory recurrence-free interval and consequently introduces immortal time bias.[26,27] Our extended model allows that the accumulated follow-up prior to pregnancy appropriately contributes to the non-pregnancy hazard estimate. The hazard ratio thus represents the risk of recurrence for a patient who has become pregnant compared to a patient who has not (but might be in the future). A multivariable model was fitted including the variables with a P-value < 0.2 in the univariable analysis. No clear method to graphically present survival curves stratified on a time-dependent variable exists. Thus, the five-year recurrence probability with 95% confidence intervals (CI) was plotted using inverted Kaplan-Meier curves, overall and stratified on hernia repair type. P-values < 0.05 were considered significant. Patients with missing data were left out only of the analyses of the concerned variable. Analyses were performed with R, version 3.1.1 (R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org/) using the packages Publish, prodlim and survival. The study was approved by the Danish Data Protection Agency (No. 2012-58-0004) and registered at clinicaltrials.gov (NCT02564757).

3. Results

In total, 3578 female patients of reproductive age underwent ventral hernia repair during the study period. Of these, 267 (7.5%) subsequently completed a pregnancy (Fig. 1). The overall median follow-up was 3.1 years (range 0–8.4 years). The median time from ventral hernia repair to pregnancy was 1.1 years (range 0–5.8 years). Patients with subsequent pregnancy were significantly younger, had smaller hernia defects, had less frequently incisional hernias, and underwent more often open repair with suture closure compared with patients without subsequent pregnancy (Table 1). Twenty-six patients underwent an additional pregnancy during follow-up (umbilical, n = 19; incisional, n = 5 and epigastric hernia repair, n = 2).

The overall ventral hernia recurrence rate was 12.5% (448 of 3578) (Table 2). Of these, 304 (67.9%) underwent reoperation for recurrence. In the multivariable extended Cox regression analysis, pregnancy was independently associated with an increased risk of ventral hernia recurrence (hazard ratio (HR) 1.56, 95% confidence interval (CI) 1.09–2.25, $P = 0.016$, Table 3). Increasing hernia defect size was likewise associated with an increased risk of recurrence (HR per 10 cm^2 increase 1.02, 95% CI 1.01–1.04, $P < 0.001$). Umbilical (HR 1.55, 95% CI 1.17–2.06, $P = 0.003$) and incisional hernia repair (HR 3.30, 95% CI 2.42–4.51, $P < 0.001$) were associated with an increased risk of recurrence compared with epigastric hernia repair. Incisional hernia repair was associated with the highest risk of recurrence compared to umbilical and epigastric hernia repair. Fig. 2 shows the overall five-year probability of ventral hernia recurrence, whilst stratification on type of hernia repair is presented in Fig. 3.

4. Discussion

In the current study subsequent pregnancy was associated with a 1.6-fold increased risk of ventral hernia recurrence in a cohort of female patients of reproductive age. Increasing hernia defect size was also identified as an independent risk factor associated with ventral hernia recurrence. Incisional and umbilical hernia repair was associated with an increased risk of recurrence compared with epigastric hernia repair.

To our knowledge, only one recent study have examined subsequent pregnancy as a risk factor for ventral hernia recurrence finding similar results.[11] In comparison with our study, data on smoking, obesity and wound complication was included, whereas adjustment for hernia defect size and surgical technique-related factors was not. Together with the present study, there is growing evidence for the pregnancy-associated increased risk of recurrence. Contrary, a previous review found two case-series reporting on 35