Long-term Results of a Randomized Controlled Trial of a Nonoperative Strategy (Watchful Waiting) for Men With Minimally Symptomatic Inguinal Hernias

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Objective: To assess the long-term crossover (CO) rate in men undergoing watchful waiting (WW) as a primary treatment strategy for their asymptomatic or minimally symptomatic inguinal hernias.

Background: With an average follow-up of 3.2 years, a randomized controlled trial comparing WW with routine repair for male patients with minimally symptomatic inguinal hernias led investigators to conclude that WW was an acceptable option [*JAMA*. 2006;295(3):285–292]. We now analyze patients in the WW group after an additional 7 years of follow-up.

Methods: At the conclusion of the original study, 254 men who had been assigned to WW consented to longer-term follow-up. These patients were contacted yearly by mail questionnaire. Nonresponders were contacted by phone or e-mail for additional data collection.

Results: Eighty-one of the 254 men (31.9%) crossed over to surgical repair before the end of the original study, December 31, 2004, with a median follow-up of 3.2 (range: 2–4.5) years. The patients have now been followed for an additional 7 years with a maximum follow-up of 11.5 years. The estimated cumulative CO rates using Kaplan-Meier analysis was 68%. Men older than 65 years crossed over at a considerably higher rate than younger men (79% vs 62%). The most common reason for CO was pain (54.1%). A total of 3 patients have required an emergency operation, but there has been no mortality.

Conclusions: Men who present to their physicians because of an inguinal hernia even when minimally symptomatic should be counseled that although WW is a reasonable and safe strategy, symptoms will likely progress and an operation will be needed eventually.

Keywords: inguinal hernia, hernia accident, minimally symptomatic, randomized controlled trial, watchful waiting

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Annually, more than 20 million inguinal herniorrhaphies are performed worldwide,[1] and it is one of the most common operations performed by general surgeons.[2] Up to one third of patients with inguinal hernias are asymptomatic or minimally symptomatic at the time of presentation.[3] Historically, surgeons have recommended repair of an inguinal hernia at diagnosis even if minimally symptomatic to avoid a hernia accident, which is defined as a bowel obstruction caused by the hernia or strangulation of the contents of the hernia, or both.[2] However, on the basis of the results of 2 recent randomized clinical trials (RCTs),[4,5] one conducted in the United Kingdom and the other in North America, watchful waiting (WW) has now become an accepted alternative to routine repair. In 2011, the longer-term results of the United Kingdom trial were published. Using Kaplan-Meier analysis, 72% of patients were predicted to crossover (CO) from WW to surgery by 7.5 years causing the authors to conclude that routine repair should be recommended for minimally symptomatic patients without medical contraindications to surgery. We now report the long-term results of the WW arm of the North American Trial.

METHODS

Data

The methods and study design used for the American College of Surgeons (ACS) hernia trial have been previously reported in detail.[5,6] In brief, after informed consent, men who were 18 years or older and had an asymptomatic or minimally symptomatic inguinal hernia were recruited from 5 different geographical locations in North America including both community and academic centers (Table 1). These patients were randomized to WW or a standard Lichtenstein open tension-free repair. Patients with female gender, undetectable hernias, symptomatic hernias, acute hernia complications, and local or systemic infection; those in ASA (American Society of Anesthesiologists) class IV; or those participating in another clinical trial were excluded from the trial. The outcomes of the trial have been published previously.[5] After completion of the trial on December 31, 2004, study participants were invited to voluntarily enroll in a registry for long-term follow-up after approval from the institutional review board (IRB) of each participant center. Because of inability to obtain IRB approval for one site (McGill University, Montreal, Quebec, Canada), this center was excluded from the registry. After informed consent, men who agreed to participate in the study were contacted by mail questionnaire in mid 2005, mid 2006, early 2008, early 2009, and late 2010. Nonresponders were contacted by phone or e-mail for additional data collection. Patients initially randomized to WW either underwent surgery during follow-up (CO group) or continued to remain in the WW group. For the CO group, the questionnaire collected information about reason for CO and details of surgery including date, side, type of surgery, whether mesh was used for the hernia repair, postoperative pain, and hernia recurrence. For those who remained in the WW group, details about their hernia including size, descent into scrotum, use of truss, and pain associated with hernia were collected. Patient satisfaction was recorded for both the groups. The questionnaire was purposely kept very short and simple and did not contain items related to quality of life or standardized instruments for pain and activity assessment to maximize compliance.

Patients

Patients assigned to the WW group in the initial RCT were divided into the CO group and WW group for this study. Baseline medical comorbidities and demographic and lifestyle variables that

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#The list of investigators of the original trial is given in Table 1.

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TABLE 1. Original Investigators and Sites of the ACS Hernia Trial

Site Investigators	Study Site	Investigator Affiliations
Robert J. Fitzgibbons, Jr, MD	Omaha, VA	Creighton University, Omaha, NE
Karen Kaczmarek, RN	NA	Creighton University, Omaha, NE. Study coordinator for the initial trial and the registry
Anita Giobbie-Hurder, MS	NA	VA Cooperative Studies Program Coordinating Center, Hines, IL
James O. Gibbs, PhD	NA	Northwestern University, Chicago, IL
Dorothy D. Dunlop, PhD	NA	Northwestern University, Chicago, IL
Domenic J. Reda, PhD	NA	VA Cooperative Studies Program Coordinating Center, Hines, IL
Martin McCarthy, Jr, PhD	NA	Northwestern University, Chicago, IL
Leigh A. Neumayer, MD	NA	Salt Lake City VA Health Care System, University of Utah, UT
Jeffrey S. T. Barkun, MD	Montreal, Canada	McGill University, Montreal, Quebec
James L. Hoehn, MD	Marshfield, WI	Marshfield Clinic, Marshfield, WI
Joseph T. Murphy, MD	Dallas, TX	University of Texas, Southwestern Medical Center at Dallas, Dallas VA Medical Center, Dallas, TX
George A. Sarosi, Jr, MD	Dallas, TX	University of Texas, Southwestern Medical Center at Dallas, Dallas VA Medical Center, Dallas, TX
William C. Syme, MD	Albuquerque, NM	Lovelace Clinic, Albuquerque, NM
Jon S. Thompson, MD	Omaha, NE	Omaha VA Medical Center, Omaha, NE
Jia Wang, MS	NA	VA Cooperative Studies Program Coordinating Center, Hines, IL
Olga Jonasson, MD	NA	University of Illinois, Chicago, IL

NA indicates not applicable.

were collected at the time of randomization in the original study are compared between the 2 groups in Table 2. All study participants in both the original and current study were males who had asymptomatic or minimally symptomatic inguinal hernias at the time of randomization. The primary outcome variable was CO to surgery and included the patients who crossed over before the end of the original study and those who crossed over during the current study. The reasons for CO and time to CO were also studied.

Statistical Analyses

Univariate exploratory analyses were performed using Pearson χ^2 test or Fisher exact test for categorical variables and student *t* test for continuous variables. Multivariate analysis using Cox proportional hazards models was carried out to assess risk factors for CO to surgery for the long-term follow-up period. Factors from the univariate analyses (Table 2) that had a $P \leq 0.4$ were included in the Cox proportional hazards regression analysis. The model selection used a backward elimination procedure and was verified by a forward selection procedure. The ties were handled by the method postulated by Efron and Bradley.[7] The proportional hazard assumption in the final model is accessed by martingale residuals for each covariate proposed by Lin et al.[8] There were no differences in the baseline characteristics and total follow-up time in the registry of patients with complete follow-up as compared with those who dropped out at various time periods; therefore, censoring of subjects was not biased as far as we know. Baseline characteristics of the hernia registry participants were compared with those of patients from the original ACS hernia study who did not participate in the registry to assess possible selection bias.

Kaplan-Meier curves were plotted for time to CO from WW to surgery. The registry participants were divided into 2 groups according to age. Log-rank test was used to compare CO times for the 2 age groups. Statistical analyses were performed using SPSS (SPSS 17.0 Inc, Chicago, IL) and SAS (version 9.2; SAS Institute, Cary, North Carolina). All analyses were performed for 2-sided tests. $P < 0.05$ was considered statistically significant.

RESULTS

In the original study, 366 (50.8%) patients of the 720 patients enrolled were randomized to WW. Of the WW group, 254 (69.4%) men enrolled in the long-term follow-up registry. Of these, 167(65.7%) subjects had complete follow-up data to the end of the study, 9 men died, 3 withdrew consent, and 75 became lost to follow-up at various times. We compared the baseline variables in the group of patients lost to follow-up and those who completed full follow-up. There were no statistical differences except the group that completed follow-up had a higher percentage of patients older than 65 years than the group that lost to follow-up. However, when we looked at risk factors for CO in all patients using cox analysis and for only the 167 patients with complete follow-up using logistic regression analysis, we found that age was a risk factor regardless of loss to follow-up or the model used. So, our results should not be affected by any directional bias overall. For the purposes of the Kaplan-Meyer analysis, the date of randomization was subtracted from the date of CO to surgery or the date of last follow-up.

Demographics, Univariate Analyses and CO to Surgery

The mean age [±standard deviation (SD)] for the CO and WW group was 58.24 (±13.03) and 54.18 (±14.38) years, respectively, ($P = 0.005$) in the original study. Eighty-three men (32.7%) were older than 65 years at the time of randomization. Patient demographics and clinical characteristics of the CO and WW groups at the time of randomization to the original study are depicted in Table 2. Patients in the WW group were significantly younger, more likely to have a chronic cough and have an alcohol intake of more than 2 drinks per day during the 2 weeks before randomization. Eighty-one men crossed over to surgery before the original study ended on December 31, 2004. By the year 2010, the number of men observed to CO from the beginning of the original study had increased to 141. Information about time to CO to surgery and reason for CO for these 141 patients was unavailable for 9 and 18 men, respectively. For the 9 men whose time to CO was unavailable, their CO time was

TABLE 2. Univariate Analyses of Patient Characteristics at Time of Randomization

Factor	CO Group, N = 141 (%)	WW Group, N = 113 (%)	P
Age, mean (±SD), y	58.24 ± 13.03	54.18 ± 14.38	0.004
BMI, mean (± SD), kg/m^2	26.46 ± 3.85	26.25 ± 3.4	NS (0.66)
Study site			
Albuquerque	38 (27)	19 (16.8)	NS (0.13)
Dallas	34 (24.1)	27 (23.9)	
Marshfield clinic	11 (7.8)	11 (9.7)	
Omaha (Creighton University)	53 (37.6)	53 (37.6)	
Omaha (University of Nebraska)	5 (3.5)	2 (1.8)	
Omaha (Omaha VA)	0	3 (1.2)	
Laterality			
Unilateral	113 (80.1)	93 (82.3)	NS (0.67)
Bilateral	28(19.9)	20 (17.7)	
Race			
White	123 (89.8)	101 (91.8)	NS (0.44)
Black	12 (8.8)	9 (8.2)	
Asian	2 (1.5)	0	
Hispanic	9 (6.4)	7 (6.2)	NS (0.94)
Employment status			
Employed	86 (61.4)	69 (61.1)	NS (0.91)
Disabled	7 (5.0)	8 (7.1)	
Retired	44 (31.4)	3 (2.1)	
Unemployed	3 (2.1)	2 (1.8)	
Self-employed	21 (24.4)	22 (31.9)	NS (0.30)
Marital status			
Single	17 (12.1)	21 (18.6)	NS (0.50)
Married	101 (72.1)	70 (61.9)	
Divorced	15 (10.7)	14 (12.4)	
Separated	3 (2.1)	3 (2.7)	
Widowed	4 (2.9)	5 (4.4)	
Education			
Grammar school	4 (2.9)	2 (1.8)	NS (0.14)
High school	37(26.4)	36 (31.9)	
College	59 (42.1)	56 (49.6)	
Postgraduate	40 (28.6)	19 (16.8)	
Annual gross household income, $			
0–19,999	12 (8.6)	18 (15.9)	NS (0.49)
20,000–39,999	43 (30.7)	32 (28.3)	
40,000–59,999	25 (17.9)	21 (18.6)	
60,000–79,999	21 (15)	9 (8)	
80,000–99,999	8 (5.7)	7 (6.2)	
≥100,000	14 (10)	9 (8)	
Does not know	11 (7.9)	10 (8.8)	
Refused	6 (4.3)	7 (6.2)	
Highest level of physical activity			
Sedentary	19 (13.6)	10 (8.8)	NS (0.80)
Light work or recreation	35 (25)	29 (25.7)	
Medium work or recreation	46 (32.9)	34 (30.1)	
Heavy work or recreation	30 (21.4)	29 (25.7)	
Very heavy work or recreation	10 (7.1)	11 (9.7)	
Private health insurance	112 (80)	88 (77.9)	NS (0.68)
Person available to help	116 (82.9)	88 (77.9)	NS (0.32)
MI within 6 mo	1 (0.7)	0	NS (1.00)
Angina	2 (1.4)	1 (0.9)	NS (1.00)
Hypertension requiring medication	32 (22.9)	30 (26.5)	NS (0.49)
CNS			
No events	135 (96.4)	110 (97.3)	NS (0.66)
History of TIA	4 (2.9)	3 (2.7)	
CVA with no residual neurological deficit	1 (0.7)	0	
Chronic constipation	5 (3.6)	4 (3.5)	NS (1.00)
More than 10% loss of body weight in last 6 mo	3 (2.1)	3 (2.7)	NS (1.00)
AIDS	0	1 (0.9)	NS (0.45)
Revascularization/ amputation for PVD	0	2 (1.8)	NS (0.2)
Claudication	0	2 (1.8)	NS (0.2)
Severe COPD	1 (0.7)	0	NS (1.00)
Chronic cough	2 (1.4)	8 (7.1)	0.046
Prostatism	22 (15.7)	10 (8.8)	NS (0.1)

(*continued*)

TABLE 2. (*Continued*)

Factor	CO Group, N = 141 (%)	WW Group, N = 113 (%)	P
DM requiring medication			
No diabetes	137 (97.9)	104 (92)	0.06
On oral hypoglycemics	3 (2.1)	6 (5.3)	
On insulin	0	3 (2.7)	
Dyspnea			
None	136 (97.1)	111 (98.2)	NS (0.69)
With minimal exertion	4 (2.9)	2 (1.8)	
Smoking in past year	19 (13.6)	25 (22.1)	NS (0.07)
Alcohol use >2 drinks per day in last 2 wks	12 (8.6)	21 (18.8)	0.02
ASA class			
1	101 (72.1)	71 (62.8)	NS (0.21)
2	33 (23.6)	38 (33.6)	
3	6 (4.3)	4 (3.5)	
Patient on aspirin	56 (40)	31 (27.4)	0.04
Patient on anticoagulants	6 (4.3)	4 (3.5)	NS (1.00)
Chemotherapy within 2 yrs	1 (0.7)	1 (0.9)	NS (1.00)
Intravenous drug use	0	1 (0.9)	NS (0.45)

P value is based on χ^2 test/Fischer exact test for categorical and *T* test for continuous variables.

CNS indicates central nervous system; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; MI, myocardial infarction; NS, not statistically significant; PVD, peripheral vascular disease; TIA, transient ischemic attack.

approximated by calculating the time from their randomization because of the last recorded follow-up date and dividing this by 365.25 days. Pain was the major reason for CO, with 54.1% reporting that it was the sole reason, and another 22.8% citing it as one of multiple reasons (Table 3). The most frequent surgery performed was unilateral open repair of hernia with mesh (Table 4). Three men (2.4%) underwent surgery for a hernia accident but there was no mortality. Two men with a hernia accident were younger than 65 years and 1 man was older than 65 years. The incidence rate of hernia accident was 0.2 per 100 person years for the whole cohort, 0.56 per 100 person years for patients younger than 65 years and 0.11 per 100 person years for patients older than 65 years.

Baseline characteristics of hernia registry participants were compared with patients from the original ACS hernia study assigned to the WW group who did not participate in the registry. Both groups had similar ($P > 0.05$) mean age, body mass index (BMI), race distribution, employment status, smoking status, alcohol use, ASA classification, and medical comorbidities. Compared with the nonregistry participants, hernia registry participants had a higher percentage of bilateral simultaneous hernia repair ($P < 0.0001$), were less likely to be Hispanic ($P = 0.05$), had a higher level of education ($P < 0.0001$), were more likely to have private health insurance ($P < 0.0001$), had pain on heavy work or recreation ($P = 0.043$), and had less hypertension ($P = 0.0352$) and less dyspnea ($P = 0.0382$).

TABLE 3. Reasons for Crossover to Surgery

Reason for CO	%
Developed more pain	54.1
Tired of having the hernia	3.3
Incarceration	2.4
Advised by doctor to have it repaired	4.1
Employer wanted hernia repaired	0.8
Other	8.1
Combination of reasons (including increased pain)	30.9

TABLE 4. Type of Surgery for the 141 Patients Who Crossed Over

Type of Surgery	N (%)
Unilateral open repair with mesh	93 (69.4)
Laparoscopic bilateral hernia repair	9 (6.7)
Open bilateral hernia repair	20 (14.9)
Laparoscopic unilateral repair	10 (7.5)
Open unilateral repair without mesh	1 (0.7)
Unsure	1 (0.7)
Missing data	7 (0.05)

Cox Proportional Hazards Regression and Kaplan-Meier Analyses

Variables from the univariate analysis with a *P* value of less than 0.4 were included in a Cox Proportional Hazards regression analyses. CO to surgery was associated with age more than 65 years [Hazard ratio (HR) = 1.77; 95% confidence interval (CI): 1.24–2.53, $P = 0.002$], a higher level of education (HR = 1.32; 95% CI: 1.06–1.64, $P = 0.012$), prostatism (HR = 1.93; 95% CI: 1.19–3.13, $P = 0.008$), and a more favorable ASA Class (HR = 0.53; 95% CI: 0.35–0.81, $P = 0.003$). Kaplan-Meier analyses (Fig. 1, Table 5) estimates that 50% of the patients CO to surgery by 7.3 years (95% CI: 5.3–8.4 years) from randomization. The estimated CO rate was 68% at 10 years from randomization. Median time to CO (Fig. 2) was shorter in men older than 65 years (3.7 years, 95% CI: 2.4–6.9 years) than in younger men (median time = 8.3 years, 95% CI: 6.6–10 years) ($P = 0.001$). Table 5 depicts the estimated cumulative CO rate by Kaplan-Meier analysis for the overall cohort and for the 2 age groups.

Contralateral, Recurrent Hernia, and Patient Satisfaction

Of the 141 total patients who crossed over during the original study and the registry follow-up, 5 men (3.55%) in the CO group developed a contralateral hernia and none had repair of the hernia. Two men (1.77%) in the WW group developed a contralateral hernia and these were managed conservatively. Four men (2.84%) developed a recurrent hernia, and 1 man had repair of the recurrent hernia. On inquiry about their satisfaction with being managed conservatively, 96 men (95%) were satisfied, 4 men (4%) were neutral, and 1 man (1%)

was dissatisfied. Among the CO group, 125 men (92.6%) were satisfied, 7 men (5.2%) were neutral, and 3 men (2.2%) were dissatisfied with surgery.

DISCUSSION

Mizrahi and Parker[9] published a systematic review of the available evidence in the literature related to the management of an asymptomatic inguinal hernia in 2012. PubMed, the Cochrane Library database, Embase, national guidelines (including the National Library of Guidelines Specialist Library), National Institute of Health and Clinical Excellence guidelines, and the National Research Register were searched using the following terms: hernia, inguinal, groin, asymptomatic, incidental, occult, and natural history. A total of 259 citations were identified with this process, but only 5 were felt to be suitable for the purposes of their review. These 5 manuscripts were the products of the main results or subanalysis of 2 prospective RCTs.[4,5] Thus, the literature dealing with the management of a minimally symptomatic hernia is made up almost exclusively from these 2 studies.

The first study was conducted by O'Dwyer and associates from the United Kingdom, and the 1-year results were published in 2006. One hundred sixty male patients with minimally symptomatic inguinal hernias 55 years or older were randomized to observation or operation. At 1 year, there were no significant differences between the groups for pain at rest or on movement. Similarly, use of analgesia was not different. At 6 months, there was significant improvement in most of the dimensions of the SF-36 quality-of-life instrument for the operation group. By 12 months, although the trend remained the same, the difference was only significant for change in health as measured by the single item in the SF-36 that provides an indication of perceived change in health. At a median follow-up of 543 days, 29% (23/80) in the observation group had crossed over to surgery with increasing pain and hernia enlargement being the most common reasons. The investigators speculated that observation may not be the best strategy for men with asymptomatic hernias because a repair did not seem to affect the rate of long-term chronic pain and the fact that patients who underwent operation perceived that their general health had improved as measured by single item in the SF-36. This is in contradistinction to the observed patients whose quality-of-life scores actually declined. The group published a long-term follow up study in 2011. They noted by Kaplan-Meyer analysis that 72% of patients would cross over to surgery by 7·5 years causing them to conclude that "there seems little point in WW because the majority of patients will require an operation in the foreseeable future" and that surgical care for an asymptomatic hernia should be recommended for medically fit patients.[10]

The second study randomizing patients with minimally symptomatic inguinal hernias to WW versus routine repair was conducted in North America and was published in 2006. It is the source for patients reported in this study. A total of 753 men with minimally symptomatic hernias were randomized to WW versus a conventional Lichtenstein herniorrhaphy. The primary aims of the study were to measure pain interfering with normal activities and physical function as measured by the physical component score of the SF-36 at 2 years. There was no difference at the 2-year mark. Twenty-three percent of patients in the WW group crossed over to surgery by 2 years, and this increased to 31% by the end of the study with an average follow-up of 3.2 years. A hernia accident defined as a bowel obstruction or strangulation of incarcerated contents occurred in 2 patients, which translated into a lifetime cumulative risk of one fifth of 1% per year. The unqualified conclusion was that WW was a safe and acceptable management strategy for men with asymptomatic or minimally symptomatic inguinal hernias.

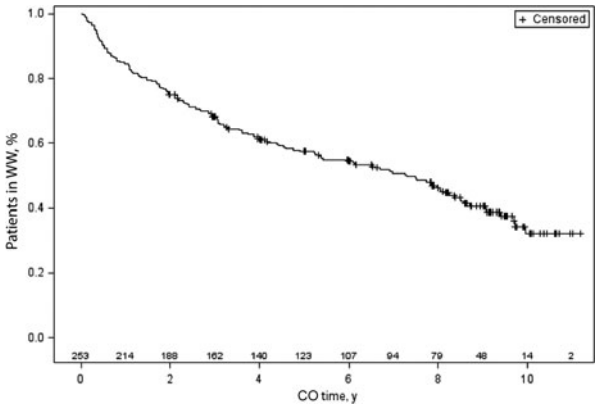

FIGURE 1. Kaplan-Meier analyses of cross over to surgery. The numbers 254, 215, 190, . . . , 4 are the number of subjects at risk at randomization, follow-up years 1, 2, . . . , 11.

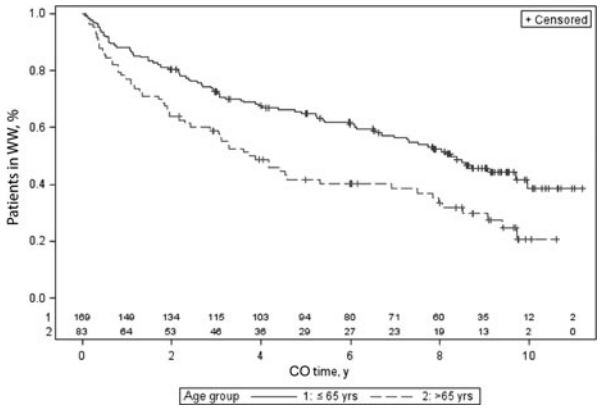

FIGURE 2. Kaplan-Meier analyses comparing CO with surgery in different age groups. The numbers 170, 150, 136, . . . , 3 are the number of subjects at risk at randomization, follow-up years 1, 2, . . . , 11 for patients with age ≤ 65 years. The numbers 83, 64, 53, . . . , 1 are the number of subjects at risk at randomization, follow-up years 1, 2, . . . , 11 for patients with age > 65 years.

TABLE 5. Estimated Cumulative CO Rates Using Kaplan-Meier Analysis

Follow-up in Years	1	2	3	4	5	6	7	8	9	10
Age ≤ 65 yrs	11.83%	19.53%	27.39%	32.53%	35.25%	38.93%	43.60%	47.60%	54.31%	61.58%
Age > 65 yrs	22.89%	36.14%	41.06%	51.35%	58.26%	59.70%	61.38%	66.42%	70.17%	79.35%
Overall cohort	15.42%	24.90%	31.76%	38.59%	42.70%	45.64%	49.35%	53.73%	59.43%	67.97%

TABLE 6. Comparison of 2 Randomized Trials on WW for Inguinal Hernia

Variable	ACS Hernia Trial	United Kingdom Trial
No. Patients	720	160
Age in years	>18 (mean = 58)	>55 (mean = 70 yrs)
Size	Any	Visible bulge
Reducibility	Not required	Required
Incarceration	0.3%	1%
CO	23% (24 mo)	26% (15 mo)

In the current study, we have analyzed the long-term results of the patients from the North American trial who had been assigned to the WW group. Using Kaplan-Meier analysis, which adjusts for those who die, withdraw, or become lost to follow-up, it can be predicted that 68% of patients will cross over to surgery by 10 years. When patients older than 65 years were studied, the estimated CO rate was 79.35% after 10 years compared to 62% in those younger than 65 years. On multivariate analyses, age more than 65 years was found to be independently associated with CO to surgery. This significant difference in CO related to age helps to explain the higher overall CO rate in the UK study. There were considerable dissimilarities in the demographics of the study populations (Table 6). The patients in the UK trial assigned to WW were 55 years or older, with a mean age of 70.9 years, whereas the patients included in the North American trial were men 18 years and older with a mean (±SD) age of 57 (±13.85) years.

On the basis of the overall CO rate of 72% at 7.5 years in the UK trial and the 68% overall CO rate by 10 years in the present study (rising to 79% in patients 65 and older), the logical assumption is that WW is not an effective strategy as with time almost all will go on to have their hernias repaired because of increasing symptoms. However, we caution that these results do not necessarily apply to the general population of patients with asymptomatic or minimally symptomatic inguinal hernias. Primary care physicians have been observing elderly patients for years and would be loath to believe a CO rate as high as is being reported here and in the UK trial. The answer may lie in the recruitment process in both studies. In an ideal world, a WW trial would be designed to screen a group of patients felt to be generalizable to the population as a whole, and then randomize all patients found to have the condition. But because of informed consent issues, this is usually not practical or ethical. In both of the studies discussed here, the majority of the subjects came to the clinic because of concern about the hernia and it was at that point they were invited to participate in the trial. Thus, it is not valid to extrapolate the conclusions to the entire population of asymptomatic or minimally symptomatic inguinal hernia patients. However, the results of these 2 trials provide overwhelming evidence that those patients who choose to attend their Doctor's office because of concerns about their hernia even if they state that symptoms are minimal or absent will almost inevitably come to surgery.

The recruitment process may also explain why the CO rate is so much higher in elderly patients. One might speculate that elderly patients have a tendency to minimize their symptoms more than younger patients and thus they become eligible for the trial despite having more advanced disease. This logic would dictate that it is not the age itself which causes the higher CO rate but rather age plus the fact that the patient goes to the trouble of attending the clinic. Again, rather than recommending that all otherwise healthy elderly patients have their asymptomatic hernias repaired as the authors of the UK trial have stated, it might be more prudent to tell patients that the high CO rate applies to patients actually attending a clinic for their hernia and may not apply to the general population of asymptomatic or minimally symptomatic hernia patients. Patients should be counseled that for those men who come to a clinic with minimal symptoms, it is safe to delay repair for several years but that increasing symptoms will more than likely cause them to choose to have their hernia repaired over the next 10 years.

In the past, the rationale to recommend surgery for asymptomatic or minimally symptomatic groin hernias has been to prevent a hernia accident (bowel obstruction or strangulation of hernia contents).[2] However, in our study, only 3 patients (2.4%) in the WW group developed incarceration for which they underwent surgery with no mortality. This is similar to the 2.5% acute presentation risk found by the UK investigators.[10] Thus, the finding that the risk of a hernia accident should not be considered an indication for surgery in and of itself in the original study was confirmed in this long-term follow-up. Older studies in the literature, which have shown higher risk of acute hernia events with increased age with an increased mortality rate, can no longer be considered relevant.[2,11–13]

Higher education level was predictive of CO to surgery. Literature studies have shown that a higher education level is associated with more involvement in medical decision making[14–16] and this could be a contributory factor for the decision to cross over to surgery.

Our study is the only one in literature that looks at the natural history of adult patients of all age groups with asymptomatic or minimally symptomatic inguinal hernias. It includes patients from different regions of North America and 5 different centers. The enrollment rate of 69% of the original patients in the WW group can be considered quite good as one of the higher accruing centers (McGill) could not provide IRB consent to participate in the registry and they had contributed 45 patients to the WW group in the original RCT. Thus, the adjusted percentage of eligible patients recruited into the registry was 79.4%.

As noted previously, the major limitation of this analysis stems from the fact that the registry was voluntary and there may be self-selection bias.[17] Our study participants came from 5 different centers, which included both academic and community hospitals. The respondents may still not be representative of the general population.

CONCLUSIONS

The results of this study show that WW remains a safe strategy even on long-term follow-up. However, patients who present to their physicians to have the hernia evaluated, especially if they are elderly, should be informed that they will almost certainly come to surgery eventually. These results should not be extrapolated to the broader population of all patients with asymptomatic or minimally symptomatic hernias.

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DISCUSSANTS

L.A. Neumayer (Salt Lake City, UT):

Dr Fitzgibbons and others know that funding a randomized clinical trial for long-term, beyond a couple of years' follow-up, is nearly impossible; thus, the need arises for a registry. However, securing funding for the registry took substantial time and effort. Without Dr Fitzgibbons' tenacity, this registry would not exist.

Understanding that background, I have several questions.

Even without the participants from the Canadian institution, which could not participate for whatever reason in the registry, the participation in the registry was good but not optimal. Overall, it was 69%, and 80% without that institution. This translates, if you put those numbers around, to a 20% to 30% nonparticipation rate. In addition, complete follow-up was only available on 167 patients. Thus, 112, or 30%, of the originally randomized patients did not participate in the registry at all, and another 87 were lost to follow-up during the duration of the registry. Both of these numbers are quite a bit higher than the 60 men who crossed over during the registry period.

Were the groups of nonparticipants and those lost to follow-ups similar to or different from the 167 with complete follow-up, at least on baseline characteristics? Did you consider conducting a sensitivity analysis to account for these high rates of nonparticipation and loss to follow-up?

Second, what data points were collected once a patient crossed over to surgery? This is important, as we showed in the laparoscopic versus open randomized trial that quality of life was lower in those patients with postoperative pain than those with a recurrence; a study spearheaded by one of our new members, Mary Hawn. Your satisfaction scores implied similar findings. There were 3 dissatisfied patients in the CO arm versus 1 in WW.

Did you use any of the standardized instruments we developed in the hernia trials to further assess these patients for outcomes?

Were the 81 patients who crossed over during the initial trial any different from the next 60?

Perhaps the biggest contribution of this registry is the ability to understand the natural history of hernias and the low rate of hernia accident. Could you give us that rate in person years? To me, this is important, especially in light of the fact that, in older patients, there was a higher CO rate, but we really need to know how to counsel patients about their risk of a hernia accident before they die of something else.

Response from R.J. Fitzgibbons (Omaha, NE):

The rate of enrollment in the trial was a problem. Since we could not get IRB approval from one of the sites to conduct the registry, the number of patients in the study were reduced. We also learned how important it is to enroll patients in a follow-up registry before completion of the original study when they still have a relationship with study personnel especially the coordinator. If you try to enroll patients after they have left the trial, there is much less cooperation. Baseline variables were compared for the group lost to follow-up versus the 167 with complete data.

On univariate analysis, there were a higher percentage of patients in the more than 65-year age group in those who completed follow-up. However, when we looked at the risk factors for CO in all patients using Cox regression, we found that age was a risk factor regardless of lost-to-follow-up status. So, our results should not be affected by directional bias overall.

Your next question dealt with what data was collected by the registry questioner. We chose a very simple data form designed to encourage cooperation and also reliability. After prolonged internal discussion among the investigators, it was decided a detailed questionnaire would be a detriment to cooperation influencing the quality of the data. So, the questioner was designed only to ask simple questions about reasons for CO and complications. For the CO group, the questionnaire collected information about reason for CO and details of surgery including date, side, type of surgery, whether mesh was used for the hernia repair, postoperative pain, and hernia recurrence. Formal questions that could have been incorporated into a quality of life type instrument were not included.

Your third question dealt with differences in the patients who crossed over during the original study versus those who crossed over during the registry. We compared the baseline variables of hernia registry participants with the nonregistry participants. Both groups were similar in mean age, race distribution, BMI, employment status, smoking status, alcohol use, ASA classification, and medical comorbidities. Compared with the nonregistry participants, hernia registry participants had a higher percentage of bilateral simultaneous hernia repair ($P < 0.0001$), were less likely to be Hispanic ($P = 0.05$), had a higher level of education ($P < 0.0001$), were more likely to have private health insurance ($P < 0.0001$), had pain on heavy work or recreation ($P = 0.043$), and had less hypertension ($P = 0.0352$) and less dyspnea ($P = 0.0382$).

Your fourth question dealt with the accident rate. In the original study, the accident rate was one fifth of 1% cumulative per year. So, by 5 years, it was 1%. If you run the numbers now, we had 1292 total hernia years, with 3 accidents. It is exactly the same. So, this has been consistent, 0.2% per year is the cumulative CO rate in both studies. This translates into 0.2 per 100 person years for the whole cohort, 0.56 per 100 person years for patients younger than 65 years and 0.11 per 100 person years for patients older than 65 years.

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V. Velanovich (Tampa, FL):

My question pertains to the physical component score of the SF 36. Have you looked at that as a preoperative predictor of who is going to end up crossing over? I would think that the patients who are more robust ahead of time would be the ones who were more likely to develop pain during that waiting period. Do you have any data on that?

Response from R.J. Fitzgibbons (Omaha, NE):

We have not actually run that particular analysis yet. One of our coinvestigators in the original study, Dr Serosi from Dallas, published a secondary paper specifically dealing with predictors of CO and we are planning to repeat this with the extended follow-up.

DISCUSSANTS

M.E. Zenilman (Bethesda, MD):

I would echo what Dr Velanovich mentioned. When I see patients who are 80 years old in the office with an asymptomatic hernia, my conversations with them are next what their lifestyle is, and if they are an active golfer, I know that they are going to end up getting their hernia fixed, because I have had a few come back. If they are sedentary, sitting at home in a retirement home, they do not.

So, I think the next step in this project really should be to find out what the activity level is of these patients who are getting older and have asymptomatic hernias.

Response from R.J. Fitzgibbons (Omaha, NE):

Again, this will be addressed in the secondary predictor's analysis, so please stay tuned.