# ORTHOPAEDIC SURGERY



# Gender, ethnicity and smoking affect pain and function in patients with rotator cuff tears

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#### Abstract

**Background:** This study is a collation of baseline demographic characteristics of those presenting for rotator cuff repair in New Zealand, and exploration of associations with preoperative function and pain. Data were obtained from the New Zealand Rotator Cuff Registry; a multicentre, nationwide prospective cohort of rotator cuff repairs undertaken from 1 March 2009 until 31 December 2010.

**Methods:** A total of 1383 patients were included in the study. This required complete demographic information, preoperative Flex-SF (functional score) and pain scores. Following univariate analysis, a multivariate model was used.

**Results:** The average age was 58 years (69% males and 11% smokers). New Zealand Europeans made up 90% and Maori 5%. The average preoperative Flex-SF was significantly lower (poorer function) in those over 65 years, females, smokers and Maori, in the non-dominant patients, using a multivariate model. Average preoperative pain scores were significantly worse (higher scores) in females, Maori, Polynesians, smokers, using a multivariate model.

**Conclusion:** This is the largest reported prospective cohort of patients presenting for rotator cuff surgery. Results can be used to understand the effect of rotator cuff tears on the different patients, for example Maori patients who are under-represented, present younger, with more pain and poorer function.

#### Introduction

The New Zealand Rotator Cuff Registry was established in March 2009 to collect prospective functional, pain and outcome data on patients undergoing rotator cuff repair in New Zealand. It is a multicentre study and all surgeons who perform rotator cuff repairs throughout New Zealand were invited to participate. To date, the registry is the largest prospective study of rotator cuff repairs in the literature.<sup>1–3</sup>

It is well documented that the incidence of rotator cuff tears increases with age.<sup>4</sup> Similarly, the influence of gender, smoking and hand dominance on the incidence of rotator cuff tears is well reported in registry and cohort studies.<sup>3,5–8</sup>

However, there is limited literature addressing the effect of demographic variables upon baseline function and pain. Some studies suggest that females have poorer functional scores preoperatively.<sup>9</sup> Smoking has been linked to lower functional scores in those waiting for rotator cuff repairs.<sup>10</sup> Hand dominance was related to higher pain scores preoperatively.<sup>11</sup> We found no literature on the relationship between race, recreational and work demands and rotator cuff tear function and pain.

The purpose of this study is to document the demographic variables of a large cohort of patients presenting for rotator cuff repairs in New Zealand, and to explore the associations between these demographics and patient functional and pain scores at baseline.

## Methods

The New Zealand Rotator Cuff Registry is a prospective multicentre registry of rotator cuff operations undertaken in New Zealand from 1 March 2009 until 31 December 2010. All surgeons who perform rotator cuff repairs throughout New Zealand were invited to participate; a total of 90 surgeons submitted data. This included primary or revision repairs, and both arthroscopic and open techniques.

Recruitment of patients to the registry was undertaken by the operating surgeon. There were 518 patients who completed enrolment questionnaires, but never completed an operative day questionnaire and were therefore excluded from the registry cohort. Figure S1 describes the exclusion and inclusion numbers. Comparative analysis of the excluded cohort showed no significant difference in age, gender, ethnicity, hand dominance and traumatic cause.

Preoperative data collection was carried out at the time of patient booking, or in the preoperative assessment clinic. Information included patient demographic questionnaire, which included age, gender, ethnicity and smoking. Traumatic cause was self-reported by the patient. Recreational and work (occupational) activity was recorded, self-reported into nil, light, medium and heavy demand. Intraoperative data collection included an operation day questionnaire filled out by the surgeon at the time of surgery.

Pain and Flex-SF scores were collected at baseline, 6, 12 and 24 months. The Flex-SF score is a validated shoulder-specific functional assessment score.<sup>12,13</sup> The set of shoulder-specific questions generates a Flex-SF score out of 50. A higher score represents better function. The pain score was generated from a self-administered questionnaire addressing average pain levels over the preceding month. Pain was scored 0–10, with a higher score representing higher pain levels.

The current study analysed certain demographic variables, and explored any associations with Flex-SF (function) and pain at baseline. Univariate analysis was carried using the Sofa statistics programme (Version 1.4.3, Paton-Simpson & Associates Ltd, Auckland, New Zealand), with *P*-values <0.05 considered statistically significant. Pearson's correlation was used to examine linear correlations, with *P*-values <0.05 considered statistically significant.

The multivariate analysis was then carried out using R software package (The R Foundation for Statistical Computing, Vienna, Austria). Values in the model included age, gender, ethnicity, smoking (yes or no), work demand (low versus high), labral tear seen at surgery (yes or no), long head of biceps pathology (damaged or subluxed, versus normal), tear size (less than and greater than 3 cm), tear retraction (less than and greater than 2 cm) and tendon quality (poor versus good).

#### Results

A total of 1383 rotator cuff repairs were analysed in the current study. Of these, 55 were revision repairs.

The average age for the registry cohort was 58 years. As shown in Table 1, the majority of patients were in the 50–59 and 60–69 age groups. Patients in over 65 years age group had lower overall baseline Flex-SF scores compared with under 65 years age group (23.6 versus 24.6, P < 0.01). As age increased, baseline Flex-SF score decreased (Pearson correlation R score: -0.07, P = 0.01). There was no linear correlation of age with pain at baseline (Pearson correlation R score: 0.02, P = 0.4). Average age in

	п	%
Age (n = 1383)		
<50	271	19.6
50–59	476	34.4
60–69	483	34.9
70–79	140	10.1
>80	13	0.9
Gender ( $n = 1383$ )		
Male	957	69.2
Female	426	30.8
Ethnicity ( $n = 1379$ )		
European	1239	89.8
Maori	74	5.4
Polynesian	20	1.5
Asian	21	1.5
Other	25	1.8
Accident ( $n = 1379$ )		
Yes	1230	89.2
No	149	10.8
Smoking status ( $n = 1379$ )		
Non-smoker	1221	88.5
Smoker	158	11.5
Work activity ( $n = 1379$ )†		
Nil	280	20.3
Low demand	329	23.9
Medium demand	388	28.1
High demand	382	27.7
Recreational activity ( $n = 1379$ ) <sup>†</sup>		
Nil	199	14.4
Low demand	526	38.1
Medium demand	487	35.3
High demand	167	12.1
Hand dominance ( $n = 1383$ )		
Dominant side	953	68.9
Non-dominant side	430	31.1
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†Work activity and recreational activity are self-reported scores of work or recreational demand, categorized into nil, low, medium or high demand.

traumatic versus atraumatic tears was significantly lower (57 years versus 61 years, P < 0.01).

Males made up 69.2% of the registry cohort. The average age of males was lower (57 years versus 59 years). Males had significantly higher Flex-SF scores compared with females (24.8 versus 23.2, P < 0.01), and significantly lower preoperative average pain scores compared with females (4.5 versus 5.3, P < 0.01), as shown in Table 2.

Ethnicity proportions are shown in Table 1. Maori (5.6 versus 4.7, P < 0.01) and Polynesians (5.7 versus 4.7, P < 0.01) had higher pain scores preoperatively, and Maori had lower preoperative Flex-SF scores (23.0 versus 24.4, P = 0.03). Average age in Maori and Polynesians was significantly lower at 51 and 49 years, respectively (P < 0.01).

The majority of the registry group were non-smokers (89%). Smokers had lower preoperative average Flex-SF scores (23 versus 24.5, P < 0.01), and higher preoperative average pain scores (5.3 versus 4.7, P < 0.01), compared with non-smokers.

The dominant hand was operated on in 68.9% of cases. Preoperative Flex-SF scores were higher in those with dominant side versus non-dominant tears (24.6 versus 23.8, P = 0.03). Work and recreational demand average Flex-SF and pain scores are shown in Table 3.

Table 2 Average pain and Flex-SF scores in relation to age, gender, ethnicity and smoking

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	Flex-SF score	P-value	Pain score	P-value
Age				
<50 50–59 60–69 70–79 >80 Gender	24.8 24.7 24.0 23.3 24.4	0.03†	4.7 4.7 4.8 4.8 5.0	0.8†
Male Female Ethnicity European	24.8 23.2 24.4	<0.01	4.5 5.3 4.7	<0.01
Maori Polynesian Asian Other Non-smoker Smoker	23.0 24.4 24.1 22.5 24.5 23.1	0.03‡ 0.9 0.8 0.09 <0.01	5.7‡ 5.7 5.1 5.4 4.7 5.3	<0.01 0.02 0.3 0.06 <0.01

†*P*-value represents trend to increasing or decreasing average Flex-SF or pain with increasing age category. ‡*P*-values represent comparison of Maori, Polynesian, Asian and other ethnicity versus European patients.

After application of the multivariate analysis, Flex-SF scores remained significantly lower for those over 65 versus under 65 (P = 0.05), females versus males (P < 0.001), smokers versus non-smokers (P = 0.01) and Maori versus Europeans (P = 0.05), but not for hand dominance or work demand. Pain scores remained significantly higher in females versus males (P < 0.001), Maori (P < 0.001) and Polynesian (P = 0.01) versus European, smokers versus non-smokers (P < 0.001) and in low demand versus high work demand patients (P = 0.01).

#### Discussion

Our study provides a demographic review of 1383 patients undergoing rotator cuff repairs throughout New Zealand undertaken by 90 different surgeons. This cohort represents patients from the

 Table 3
 Average pain and Flex-SF scores in relation to hand dominance, accident, work and recreational demand

	Flex-SF score	<i>P</i> -value	Pain score	<i>P</i> -value
Dominant hand Non-dominant hand Accident	24.5 23.9	0.04	4.8 4.6	0.05
Yes No Work activity†	24.3 24.8	0.3	4.7 4.9	0.4
Nil or low demand Medium or high demand Recreational	24.1 24.4	0.3	4.7 4.8	0.06
activity† Nil or low demand Medium or high demand	23.1 25.7	<0.01	5.0 4.5	<0.01

†Work activity and recreational activity are self-reported scores of work or recreational demand, categorized into nil, low, medium or high demand.

New Zealand Rotator Cuff Registry. Other rotator cuff registries include: the Arthroscopic Rotator Cuff Registry of New York of just under 200 patients, which is arthroscopic only, single institution, but multisurgeon<sup>2</sup> and the Finnish Registry, which includes 576 primary arthroscopic rotator cuff repairs from a single institution.<sup>14</sup> To date, the New Zealand Rotator Cuff Registry is the largest study, including both open and arthroscopic repairs.

Average age of our study group was 58 years, which is comparable to most other rotator cuff repair cohorts or registry groups.<sup>1,3,8</sup> It is however 5 years younger than that quoted in a recent article from the Multicentre Orthopaedic Outcomes Network (MOON) group review of just under 400 rotator cuff patients, who averaged 63 years.<sup>9</sup>

The highest numbers are represented in the age ranges of 50-59 and 60–69, with a large drop off in the older age ranges. The overall incidence of rotator cuff disease increases with age.7,15,16 Our study represents those with rotator cuff tears who undergo repair, so a decrease in the older age categories in likely due to lower intervention rates in this group. A large epidemiological study from the United Kingdom similarly found the highest incidence in the 55-59 age group in those presenting to medical services with rotator cuff pathology.<sup>17</sup> There was a significant linear trend to decreasing Flex-SF scores (poorer function) with increasing age. This decline with age may just represent a normal age-related variation. There are no data available for Flex-SF, but other shoulder outcome scores do vary with age and are modified accordingly.<sup>15,18,19</sup> In those over 80 years, there was a noted improvement in Flex-SF scores (non-significant) suggesting that those presenting for surgery are a high functioning portion of that age group. However, when isolating patients over 65 years, they did have lower overall Flex-SF scores compared with patients under 65 years, contrary to findings from other series.9,10

Our paper was consistent with most registry papers in that rotator cuff tears are more common in males.<sup>3,20</sup> Our study population had almost 70% males, which is higher than most other groups.<sup>1,3,8</sup> Males were significantly younger by 2 years.

The literature on functional scores and demographics is mixed. As discussed, our study had significantly higher functional scores in males, although by only one Flex-SF point. As discussed below, the clinically important difference for Flex-SF has been estimated at 3 points.<sup>12</sup> Our finding is contrary to the MOON group which found that females had higher functional scores at baseline.<sup>9</sup> Other smaller studies have found small or no differences in functional scores in favour of males.<sup>10,19</sup>

The percentage of smokers in our study was low at 11%. This is slightly lower than the current national rate of 15%.<sup>21</sup> Other registry or large prospective groups report smoking rates of between 20% and 42%,<sup>8,14,18,22</sup> with only the MOON group having a similar rate of 10%.<sup>9</sup> Smoking rates may vary due to differing definitions of smoking. Our rates are current self reported smoking, whereas some report current or recent use.

In our group, the smokers had small but significantly lower functional scores and higher pain scores than non-smokers. The negative effect of smoking and rotator cuff tears is well established, with most studies finding a strong association of smoking with incidence of rotator cuff tears.<sup>5,6</sup> The effect on function is less clear, McRae *et al.* found a negative effect on function in those waiting for repairs;<sup>10</sup> however, the MOON group found no difference.<sup>9</sup>

Several studies report ethnicity differences in those with rotator cuff tears, with most heavily in favour of Caucasian (77-98%).<sup>7,11</sup> Our cohort is similarly weighted towards the New Zealand European (Caucasian) population with 90.1%, with underrepresentation of indigenous Maori 5.3%, Polynesian 1.5%, Asian 1.5%. This compares to the New Zealand population census figures from 2013, New Zealand European 74%, Maori 15%, Polynesian 7%, Asian 12%.<sup>21</sup> This difference is not fully explained by lower incidence in these populations. In our group, Maori present younger, with significantly poorer functional scores, and higher pain scores at baseline compared with non-Maori. This is mirrored in the arthroplasty setting, both locally and internationally. Maori present later and with more severe hip and knee arthritis, despite a similar incidence of disease.<sup>23</sup> In the United States, there is a marked ethnic variation with arthroplasty, particular in older age groups.<sup>24</sup> Reasons are likely multifactorial, including access, willingness to undergo surgery, co-morbidities and socioeconomic factors.24-26

Almost 90% patients in our study reported an accident as the cause of their rotator cuff tear. This is much higher than other reports of traumatic rotator cuff tears in the literature.<sup>1,27</sup> Our study was similar to the Finland Registry, and relied on the patient self-reporting a traumatic cause.<sup>1</sup> In New Zealand, medical costs related to accidental injury are covered by a government-funded agency, the Accident Compensation Corporation. Therefore, if a tear is approved as traumatic or injury related then surgery can be undertaken in both the private and public sectors. This higher reported numbers of traumatic tears may therefore reflect not only an improved access to surgical services, but also a positive reporting bias as surgery is more likely to be funded if reported as traumatic.

Tempelhof *et al.* and Milgrom *et al.* concluded that type or physicality of work showed no association with risk of rotator cuff tear, both of these studies being in asymptomatic patients.<sup>7,15</sup> In our study group, 56% reported medium or high work demands and 48% reported medium or high recreational demands, representing a high motivation for these patients to present for surgery. High recreation demand was associated with higher functional scores, but also seemed to be protective for pain, with lower scores noted in the higher demand patients.

The results of this study must be considered after review of its inherent limitations. The subjects in this study represent a cohort of patients with rotator cuff tears who progressed to surgical repair. Ninety surgeons participated in this registry, who represent approximately 40% of all orthopaedic surgeons registered with the New Zealand Orthopaedic Association at the time of collection. Although we encouraged participation in the registry, enrolment was completely reliant on the operating surgeons. As with other voluntary sampling methods, we can never rule out selection bias. We know that there are a number of surgeons who recorded rotator cuff repair data in the operating day questionnaire but unfortunately never enrolled patients into the registry. The true number of these is unclear, as is the true number of overall rotator cuff surgeries in New Zealand in the given timeframe. Enrolment criteria included completion of a demographic questionnaire; therefore, we are unable to compare the demographic characteristics of the unenrolled patients as there is no information available. We hoped that by collecting a large number of patients from multiple centres across New Zealand a wide and varied cohort will be produced, but we can never be sure that this will be a true representation of all rotator cuff repairs in New Zealand.

The timing of collection was not linked to the operation day. It was expected that the baseline scores were collected at the time of pre-assessment clinic. This would give a short time between baseline scores and operation day. Surgical delay could have led to a larger time between scores and surgery; however, this information is not available.

When looking at significant differences in functional and pain scores, clinical significance needs to be considered. Most of the work undertaken on the Flex-SF scoring has compared clinically important differences between interventions. Work by Cook *et al.* has estimated the clinically important difference for Flex-SF to be approximately 3 points.<sup>12</sup> However, there are no data to suggest a clinically important differences in baseline function. The statistically significant differences in baseline function mentioned in the current paper need to be interpreted in context.

#### Conclusion

This study presents demographic information about the largest available prospectively followed cohort of patients undertaking rotator cuff surgery. New Zealand Europeans dominate our data set, with under-representation of Maori, Polynesian and Asian populations. Maori present younger, and with higher pain and lower functional scores. It highlights certain groups, for example older patients, females, Maori, smokers who have poorer function and pain scores. This information can be used to further understand the effect of rotator cuff tears on certain patient groups.

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#### References

- Kukkonen J, Joukainen A, Itälä A, Äärimaa V. Operatively treated traumatic versus non-traumatic rotator cuff ruptures: a registry study. Ups. J. Med. Sci. 2013; 118: 29–34.
- Nho SJ, Shindle MK, Adler RS, Warren RF, Altchek DW, MacGillivray JD. Prospective analysis of arthroscopic rotator cuff repair: subgroup analysis. J. Shoulder Elbow Surg. 2009; 18: 697–704.
- Romeo AA, Hang DW, Bach BR, Shott S. Repair of full thickness rotator cuff tears. Gender, age, and other factors affecting outcome. *Clin. Orthop. Relat. Res.* 1999; 367: 243–55.
- Yamamoto A, Takagishi K, Osawa T, Yanagawa T, Nakajima D, Shitara H. Prevalence and risk factors of a rotator cuff tear in the general population. J. Shoulder Elbow Surg. 2010; 19: 116–20.
- Baumgarten KM, Gerlach D, Galatz LM, Teefey SA, Middleton WD, Ditsios K. Cigarette smoking increases the risk for rotator cuff tears. *Clin. Orthop. Relat. Res.* 2010; 468: 1534–41.

- Kane SM, Dave A, Haque A, Langston K. The incidence of rotator cuff disease in smoking and non-smoking patients: a cadaveric study. *Orthopedics* 2006; 29: 363–6.
- Milgrom C, Schaffler M, Gilbert S, van Holsbeeck M. Rotator-cuff changes in asymptomatic adults. The effect of age, hand dominance and gender. J. Bone Joint Surg. Br. 1995; 77: 296–8.
- Nho SJ, Brown BS, Lyman S, Adler RS, Altchek DW, MacGillivray JD. Prospective analysis of arthroscopic rotator cuff repair: prognostic factors affecting clinical and ultrasound outcome. *J. Shoulder Elbow Surg.* 2009; 18: 13–20.
- Harris JD, Pedroza A, Jones GL. Predictors of pain and function in patients with symptomatic, atraumatic full-thickness rotator cuff tears: a time-zero analysis of a prospective patient cohort enrolled in a structured physical therapy program. *Am. J. Sports Med.* 2012; 40: 359–66.
- McRae S, Leiter J, Walmsley C, Rehsia S, Macdonald P. Relationship between self- reported shoulder function/quality of life, body mass index, and other contributing factors in patients awaiting rotator cuff repair surgery. J. Shoulder Elbow Surg. 2011; 20: 57–61.
- Keener JD, Steger-May K, Stobbs G, Yamaguchi K. Asymptomatic rotator cuff tears: patient demographics and baseline shoulder function. *J. Shoulder Elbow Surg.* 2010; **19**: 1191–8.
- Cook KF, Roddey TS, O'Malley KJ, Gartsman GM. Development of a Flexilevel Scale for use with computer-adaptive testing for assessing shoulder function. J. Shoulder Elbow Surg. 2005; 14 (1 Suppl. S): 90S–4S.
- Schmidt S, Ferrer M, Gonzalez M *et al.* Evaluation of shoulder-specific patient-reported outcome measures: a systematic and standardized comparison of available evidence. *J. Shoulder Elbow Surg.* 2014; 23: 434–44.
- Kukkonen J, Kauko T, Virolainen P, Äärimaa V. Smoking and operative treatment of rotator cuff tear. *Scand. J. Med. Sci. Sports* 2012; 24: 400–3.
- Tempelhof S, Rupp S, Seil R. Age-related prevalence of rotator cuff tears in asymptomatic shoulders. J. Shoulder Elbow Surg. 1999; 8: 296–9.
- Yamaguchi K, Ditsios K, Middleton WD, Hildebolt CF, Galatz LM, Teefey SA. The demographic and morphological features of rotator cuff disease. A comparison of asymptomatic and symptomatic shoulders. *J. Bone Joint Surg. Am.* 2006; **88**: 1699–704.
- White JJE, Titchener AG, Fakis A, Tambe AA, Hubbard RB, Clark DI. An epidemiological study of rotator cuff pathology using The Health Improvement Network database. *Bone Joint J.* 2014; **96-B**: 350–3.
- Carbone S, Gumina S, Arceri V, Campagna V, Fagnani C, Postacchini F. The impact of preoperative smoking habit on rotator cuff

tear: cigarette smoking influences rotator cuff tear sizes. J. Shoulder Elbow Surg. 2012; 21: 56-60.

- Ekeberg OM, Bautz-Holter E, Juel NG, Engebretsen K, Kvalheim S, Brox JI. Clinical, socio-demographic and radiological predictors of short-term outcome in rotator cuff disease. *BMC Musculoskelet. Disord.* 2010; 11: 239.
- Gulotta LV, Nho SJ, Dodson CC, Adler RS, Altchek DW, MacGillivray JD. Prospective evaluation of arthroscopic rotator cuff repairs at 5 years: part I – functional outcomes and radiographic healing rates. J. Shoulder Elbow Surg. 2011; 20: 934–40.
- Statistics New Zealand. 2013 Census QuickStats about National Highlights [PDF on Internet]. Wellington: Statistics New Zealand. [Updated Dec 2013, Cited 10 Dec 2014]. Available from URL: http://www.stats. govt.nz/Census/2013-census/profile-and-summary-reports/quickstatsabout-national-highlights.pdf
- Mallon WJ, Misamore G, Snead DS, Denton P. The impact of preoperative smoking habits on the results of rotator cuff repair. J. Shoulder Elbow Surg. 2004; 13: 129–32.
- Singleton N, Buddicom E. Are there differences between Maori and non-Maori patients undergoing primary total hip and knee arthroplasty surgery in New Zealand? A registry-based cohort study. N. Z. Med. J. 2012; 126: 23–30.
- Dunlop DD, Manheim LM, Song J *et al.* Age and racial/ethnic disparities in arthritis-related hip and knee surgeries. *Med. Care* 2008; 46: 200–8.
- Allen KD, Golightly YM, Callahan LF *et al.* Race and sex differences in willingness to undergo total joint replacement: the Johnston County Osteoarthritis Project. *Arthritis Care Res.* 2014; 66: 1193–202.
- Zhang W, Lyman S, Boutin-Foster C *et al.* Racial and ethnic disparities in utilization rate, hospital volume, and perioperative outcomes after total knee arthroplasty. *J. Bone Joint Surg. Am.* 2016; **98**: 1243–52.
- Tashjian RZ, Henn RF, Kang L, Green A. The effect of comorbidity on self-assessed function in patients with a chronic rotator cuff tear. *J. Bone Joint Surg. Am.* 2004; 86-A: 355–62.

## **Supporting information**

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Figure S1. Flow chart for inclusion and exclusion of sample sizes.