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Selective versus routine patch metal allergy testing to select bar material for the Nuss procedure in 932 patients over 10 years

Robert J. Obermeyer [a,b,*], Sheema Gaffar [b], Robert E. Kelly Jr. [a,b], M. Ann Kuhn [a,b], Frazier W. Frantz [a,b], Margaret M. McGuire [a,b], James F. Paulson [a,b,c], Cynthia S. Kelly [a,b]

[a] Children's Hospital of the King's Daughters, Norfolk, VA, USA
[b] Eastern Virginia Medical School, Norfolk, VA, USA
[c] Old Dominion University, Norfolk, VA, USA

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ABSTRACT

Aim of the study: The aim of the study was to determine the role of patch metal allergy testing to select bar material for the Nuss procedure.
Methods: An IRB-approved (11–04-WC-0098) single institution retrospective, cohort study comparing selective versus routine patch metal allergy testing to select stainless steel or titanium bars for Nuss repair was performed. In Cohort A (9/2004–1/2011), selective patch testing was performed based on clinical risk factors. In Cohort B (2/2011–9/2014), all patients were patch tested. The cohorts were compared for incidence of bar allergy and resultant premature bar loss. Risk factors for stainless steel allergy or positive patch test were evaluated.
Main results: Cohort A had 628 patients with 63 (10.0%) selected for patch testing, while all 304 patients in Cohort B were tested. Over 10 years, 15 (1.8%) of the 842 stainless steel Nuss repairs resulted in a bar allergy, and 5 had a negative preoperative patch test. The incidence of stainless steel bar allergy (1.8% vs 1.7%, $p = 0.57$) and resultant bar loss (0.5% vs 1.3%, $p = 0.23$) was not statistically different between cohorts. An allergic reaction to a stainless steel bar or a positive patch test was more common in females (OR = 2.3, $p < 0.001$) and patients with a personal (OR = 24.8, $p < 0.001$) or family history (OR = 3.1, $p < 0.001$) of metal sensitivity.
Conclusion: Stainless steel bar allergies occur at a low incidence with either routine or selective patch metal allergy testing. If selective testing is performed, it is advisable in females and patients with a personal or family history of metal sensitivity. A negative preoperative patch metal allergy test does not preclude the possibility of a postoperative stainless steel bar allergy.
Level of evidence: Level III Treatment Study and Study of Diagnostic Test.
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The Nuss procedure is performed with either stainless steel or titanium bars that are alloys of various elements [1]. (Table 1). Allergies to the elements in stainless steel, especially nickel, have a reported prevalence of 10–15% in the general population [2,3]. A preoperative metal allergy test (PMAT) is a dermally applied test performed in some centers to screen for a stainless steel allergy. A PMAT can be performed with individual topical elements but the majority are performed with commercially available products (e.g., T.R.U.E.™ (Thin-layer Rapid Use Epicutaneous patch), AllergEAZE™) that screen for multiple elements in the stainless steel bar (SSB) [4–6]. Positive results necessitate the use of the alternative titanium bar for Nuss repair. While the routine use of titanium bars for Nuss repair would decrease the incidence of bar allergies, there are several disadvantages associated with its use including a substantial cost increase [1].

Our initial screening strategy to evaluate for a potential SSB allergy required PMAT in a select group of patients considered to be at risk based on clinical variables. All other patients had stainless steel bars placed without testing. Using this strategy several patients repaired with stainless steel bars developed an allergy, therefore routine PMAT testing was recommended as a strategy to prevent this adverse outcome [7]. This study aims to compare the outcomes of selective versus routine metal allergy testing and identify clinical risk factors predictive of a stainless steel bar allergy.

1. Methods

An IRB-approved, single institution, retrospective cohort study comparing selective and routine patch metal allergy testing of 932 patients undergoing primary Nuss repair over a 10-year period (9/2004–9/2014) was performed.

Cohort A (9/2004–1/2011), PMAT was performed selectively on patients who reported a personal history or first-degree family history

* Corresponding author at: Children's Hospital of the King's Daughters, 601 Children's Lane, Norfolk, VA, 23509, USA. Tel.: +1 757 668 7703; fax: +1 757 668 8860.
E-mail address: Robert.Obermeyer@chkd.org (R.J. Obermeyer).

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Table 1
Components of stainless steel and titanium bars (Biomet[tm]).

Stainless steel bar		Titanium bar	
Inorganic element	% Composition	Inorganic element	% composition
Chromium (Cr)	17–19	Aluminum (Al)	5.5–6.75
Nickel (Ni)	13–15	Vanadium (V)	3.5–4.5
Molybdenum (Mo)	2.25–3.0	Iron (Fe)	0.3
Manganese (Mn)	2	Yttrium (Y)	0.005
Copper (Cu)	0.5	Titanium (Ti)	Balance
Trace	0–0.3		
Iron (Fe)	Balance		

of metal sensitivity and those with multiple food, drug, or environmental allergies. Patients without these clinical risk factors had stainless steel bars placed without a PMAT. A small number of patients had titanium bars placed without a PMAT. These patients were excluded from the statistical analysis since their true stainless steel allergy status could not be confirmed.

Cohort B (2/2011–9/2014), all patients underwent PMAT. Patients with a positive test received titanium bars and patients with a negative test received stainless steel bars. Only patients that underwent primary Nuss repair and completed therapy with bar removal were included in the study.

In order for a patient to be categorized as having a SSB allergy in this study the patient either had to have a positive PMAT at any time or allergic symptoms after stainless steel bar placement that improved with steroids or bar removal. The cohorts were compared for the incidence of bar allergies and resultant premature bar loss. In addition, demographic risk factors for a reaction to the elements of stainless steel in a dermal patch test or a stainless steel bar allergy were examined. One-tailed Fisher's exact test was used to analyze statistical significance of categorical variables. chi-Square test and logistic regression were used to produce odds ratios in the statistical analysis of risk factors.

2. Results

In cohort A, 63 (10.0%) of the 628 patients were selected for a PMAT based on clinical risk factors. Only one of the 37 patients with a negative PMAT developed a SSB allergy. There were 565 patients in this cohort that did not have a PMAT and underwent Nuss repair with a SSB (Fig. 1). Ten (1.8%) of these patients developed a SSB allergy (Table 2). In cohort B, all 304 patients had a PMAT and 64 (21.1%) tested positive requiring a titanium bar repair. The remaining 240 patients had a negative PMAT and underwent repair with a SSB (Fig. 2). Four (1.7%) of these patients developed a SSB allergy. (Table 2)

Over 10 years, 90 patients had titanium bars placed with no allergic events, while 842 patients had stainless steel bars placed with 15 (1.8%) developing a bar allergy. Notably, 5 of the 15 patients that developed a SSB allergy had a negative PMAT (Figs. 1 and 2). The incidence of a stainless steel bar allergy (1.8% vs 1.7%, $p = 0.57$) and resultant premature bar loss (0.5% vs 1.3%, $p = 0.23$) was not statistically different between cohorts. Only 6 (0.7%) of the 842 stainless steel bars placed over 10 years required premature bar removal due to a bar allergy (Table 3).

The mean time for symptoms of a SSB allergy to be recognized was 22 weeks (range 2–52 weeks). Pain (73%), peri-incisional erythema (60%), persistent lethargy (33%), and shortness of breath (33%) were the most common symptoms. Bar preservation was achieved in 9 (69%) of the 13 patients who agreed to undergo steroid therapy (Table 2). Nickel was the most common cause for a SSB allergy in our series (80%) and the most common allergen detected by dermal patch testing (61%), but other elements were also associated with SSB allergies (Table 4).

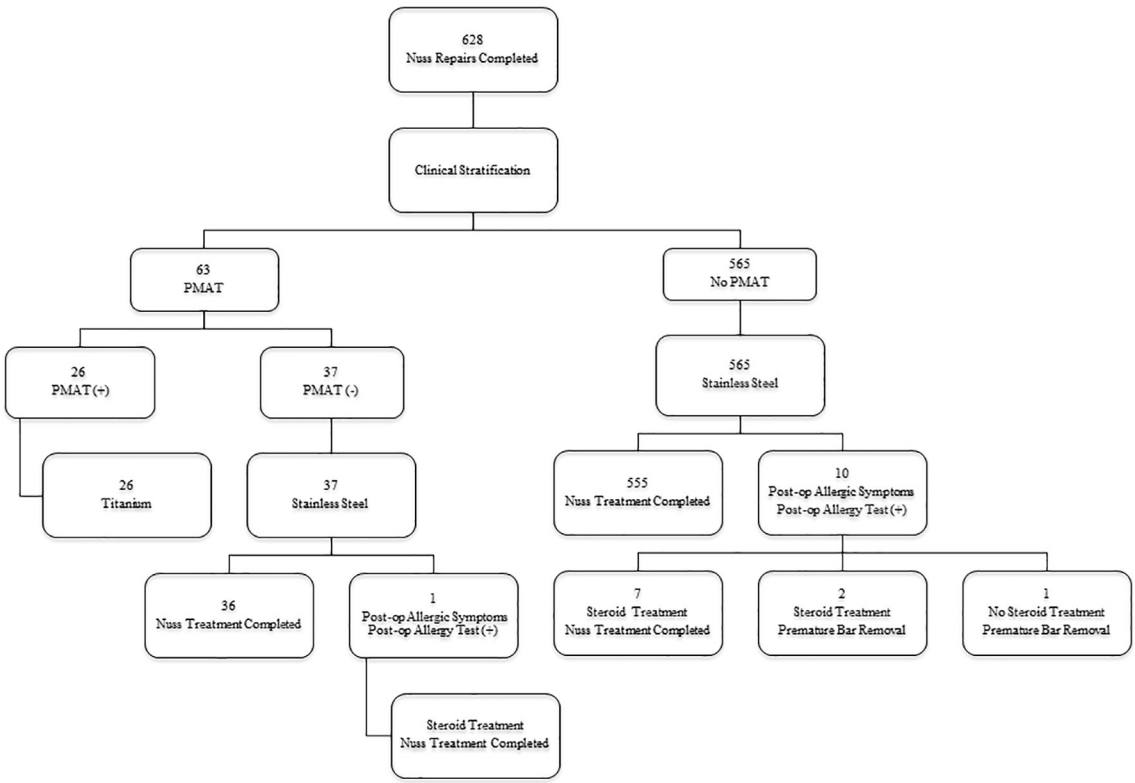

Fig. 1. Cohort A: Selective Metal Allergy Testing (9/2004–1/2011). PMAT = Pre-operative Metal Allergy Test.

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Table 2
Details of post-operative bar allergy patients.

Cohort	Onset of Symptoms Post-Op (weeks)	Symptoms									Metal Allergy	Steroid Therapy	Premature Stainless Steel Bar Removal	Timing of Stainless Steel Bar Removal	Titanium Bar Exchange
		Pain	Peri-incisional erythema	Persistent lethargy	Shortness of breath	Rash	Chronic drainage	Non-healing wound	Fever	Weight loss	Pericardial effusion				
A	32	X	X			X						(+) Ni	Yes	No	2y 8 m	No
A	2	X	X		X							(+) Ni	Yes	No	3y 0 m	No
A	5		X						X			(+) Ni	Yes	No	3y 0 m	No
A	6	X			X	X						(+) Ni	Yes	No	3y 4 m	No
A	12	X			X					X		(+) Ni	Yes	No	2y 11 m	No
A	12	X	X									(+) Ni	Yes	No	2y 6 m	No
A	16	X										(+) Ni	Yes	No	2y 5 m	No
A	24	X	X	X								(+) Ni	Yes	No	2y 6 m	No
A	14		X	X								(+) Co*	Yes	Yes	5 m	No
A	36	X	X	X								(+) Ni	Yes	Yes	1y 7 m	No
A	52		X				X	X				(+) Ni	No	Yes	1y 6 m	No
B	16	X	X	X		X	X					(+) Cu, (+) Cr, (+) Mg*	Yes	Yes	5.5 m	No
B	28				X						X	(+) Ni	No	Yes	9 m	Yes
B	50	X					X	X				(+) Ni	Yes	Yes	1y 0 m	Yes
B	3	X		X	X	X						None	Yes	No	2y 8 m	No

* Cobalt and magnesium are not components of the stainless steel bar.

Personal history of metal sensitivity, first-degree family history of metal sensitivity, history of environmental allergies, food allergies, drug allergies and sex were analyzed for statistical significance as risk factors for a positive PMAT and SSB allergy. Of the 367 patients that had a PMAT in the examined decade, only personal history of metal sensitivity ($OR = 8.6$; $p < 0.001$) predicted a positive result (Table 5). Patients with a positive PMAT or a SSB allergy were compared to those who received a SSB without an allergic event. This analysis identified females ($OR = 2.3$; $p < 0.001$) and patients with a personal ($OR = 24.8$; $p < 0.001$) or family history ($OR = 3.1$; $p < 0.001$) of metal sensitivity to be at risk for a SSB allergy (Table 6).

3. Discussion

Although routinely placing titanium bars in patients has the potential to decrease the need for a PMAT and subsequent Nuss bar allergies, there are multiple other factors to consider when discussing this option. First, while titanium is a suitable option for patients that are allergic to stainless steel, it is not a completely inert metal and there are reports of allergies to titanium [8,9]. Second, the inherent rigidity of titanium makes them more difficult to handle than the more malleable stainless steel bars. For example, any intra-operative adjustment and bending required is much more difficult during insertion and removal. Also, increased bar rigidity has the potential to be less comfortable than stainless steel bars for patients postoperatively. Finally, titanium is associated with about a 4-fold cost increase due to materials and fees associated with computer-assisted mechanical bending by the manufacturer [1,4,10].

Routine metal allergy testing is also more costly without any improved outcomes appreciated. More dermal patch tests were administered in cohort B than in cohort A (304 vs 63) and a much higher percentage of patients had a positive PMAT in cohort B than cohort A (21.1% vs 4.1%). This overt increased incidence of positive PMAT underscores a very probable decrease in the positive predictive value of this test in our series. Ultimately, this likely resulted in an over-utilization of titanium bars in our routinely patch tested cohort without lowering the stainless steel bar allergy rate. The limitations of dermal patch testing also need to be considered since some patients developed a SSB allergy even after a negative PMAT. This may be due to a false-negative PMAT result or metal sensitization after SSB placement. Reactions that occur earlier may be due to the former while those occurring later may be due to the latter [1,2,7,10].

While a PMAT has its limitations, we sought to identify demographics that should be considered for preoperative patch metal allergy testing by analyzing the known results of all our dermal metal allergy tests and patients with and without stainless steel bar allergies over the entire study period. Personal history of metal sensitivity was a statistically significant risk factor for a positive patch test (Table 5). Personal history, family history, and female gender were statistically significant risk factors for a reaction to dermal metal allergy testing or the stainless steel bar (Table 6). This suggests that if routine metal allergy testing is not the surgeons preferred strategy, selective metal allergy testing should be performed on females and patients with a personal or family history of metal sensitivity [11,12].

When a patient present postoperatively with wound concerns a careful exam of the incision and surrounding skin is important. If there is wound drainage cultures should be obtained. Noting development and progression of a rash is important since bar allergy and adhesive allergy can be difficult to distinguish initially based on appearance alone. Contact dermatitis due to adhesive allergy usually produces a limited local reaction in the more immediate post-operative period, while a metal allergy often produces a more diffuse erythematous rash (Fig. 3) in the early or even late post-operative period. Symptoms of persistent pain, lethargy, and shortness of breath are also associated with a metal allergy. If there is clinical concern about a bar allergy

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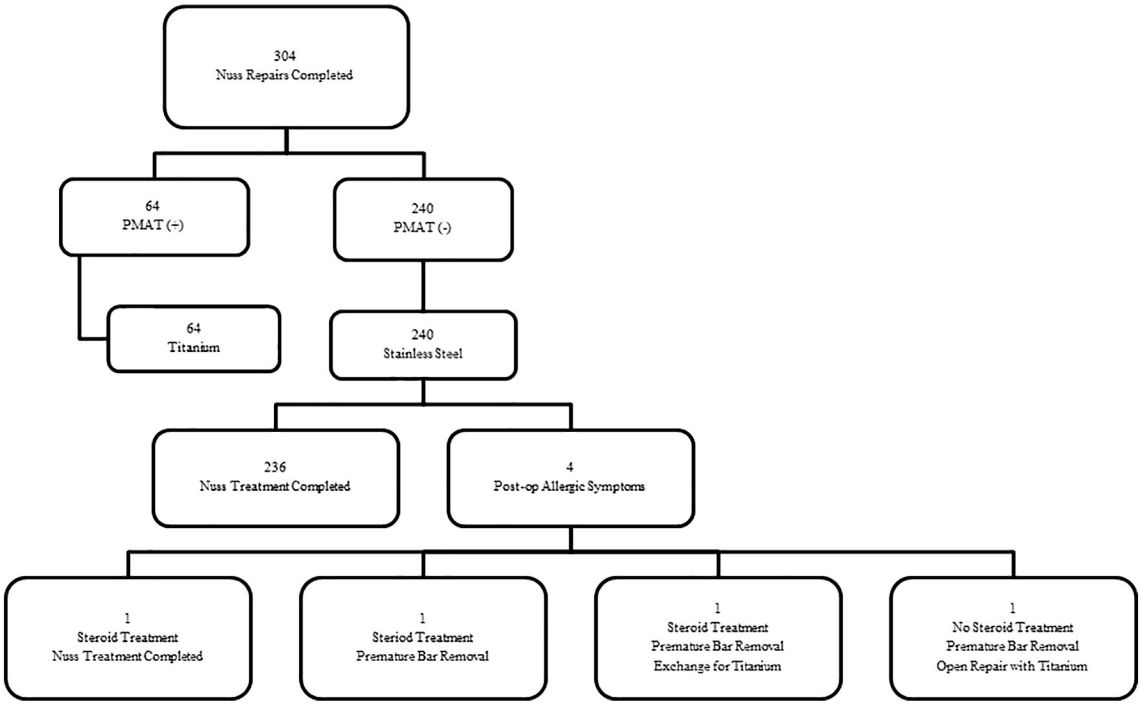

Fig. 2. Cohort B: Routine Metal Allergy Testing (2/2011–9/2014). PMAT = Pre-operative Metal Allergy Test.

then metal allergy testing should be performed as part of the workup, even if the PMAT was negative [1,4,13].

Treatment of a stainless steel bar allergy has been described to include watchful waiting for mild cases, suppressive steroids for more advanced cases, and even SSB removal with or without titanium bar replacement for failure of medical therapy [1,4,7]. The treatment course in our series was variable with an overall bar preservation rate of 60%. Of note, the bar preservation rate improved to 69% when evaluating only those patients that were treated with steroids. There was significant variation in the actual steroid regimen used in our series and an evaluation of the efficacy of the various steroid regimens is beyond the scope of this study but worth future investigation. Consulting an Allergist/Immunologist to optimize treatment is recommended.

In conclusion, stainless steel bar allergies occur at a low and clinically equivalent incidence following either routine or selective patch metal allergy testing. If selective testing is the preferred approach to workup patients for a potential stainless steel bar allergy, it is highly advisable in females and patients with a personal or family history of metal sensitivity. Repeat patch metal allergy testing should be performed if there is a clinical concern of a stainless steel bar allergy even if preoperative testing was negative.

Table 3
Cohort comparison.

Cohort	A	B	Total
Pectus repairs	628	304	932
Titanium bar repairs	26	64	90
Stainless steel bar (SSB) repairs	602	240	842
SSB allergies	11 (1.8%)*	4 (1.7%)*	15 (1.8%)
SSB premature loss	3 (0.5%)**	3 (1.3%)**	6 (0.7%)

(*p Value = 0.57; **p value = 0.23; One-tailed Fisher's exact test).

Table 4
Incidence of allergies to specific metals.

Metal	% Reactions* (n = 130)
Nickel	60.8% (79)
Chromium	15.4% (20)
Copper	15.4% (20)
Manganese	3.1% (4)
Molybdenum	2.3% (3)
Cobalt	1.5% (2)**
Magnesium	0.8% (1)**

* Any dermal testing including AllergEAZE™, T.R.U.E.™, or other.
** Cobalt and magnesium are not components of the stainless steel alloy.

Table 5
Risk Factors For Positive Preoperative Metal Allergy Test.

Demographics	(+)PMAT (n = 90)	(−)PMAT (n = 277)	p Value	Odds Ratio
M	61 (67.8%)	213 (76.9%)		
F	29 (32.2%)	64 (23.1%)	0.08	
Personal history metal sensitivity	35 (38.9%)	19 (6.9%)	<0.001	8.6
Family history metal sensitivity	14 (15.6%)	36 (13.0%)	0.54	
Environmental allergies	29 (32.2%)	93 (33.6%)	0.81	
Food allergies	9 (10.0%)	20 (7.2%)	0.37	
Drug allergies	20 (22.2%)	49 (17.7%)	0.34	

PMAT = Pre-operative Metal Allergy Test.

Table 6
Risk Factors For Positive Metal Allergy Test or Stainless Steel Bar Allergy.

Demographics	Stainless Steel Allergic (n = 105)	Non-Stainless Steel Allergic (n = 827)	p Value	Odds Ratio
M	71 (67.6%)	683 (82.6%)		
F	34 (32.4%)	144 (17.4%)	<0.001	2.3
Personal history metal sensitivity	40 (38.1%)	20 (2.4%)	<0.001	24.8
Family history metal sensitivity	14 (13.3%)	39 (4.7%)	<0.001	3.1
Environmental allergies	35 (33.3%)	311 (37.6%)	0.393	
Food allergies	8 (7.6%)	54 (6.5%)	0.673	
Drug allergies	24 (22.9%)	148 (17.9%)	0.217	

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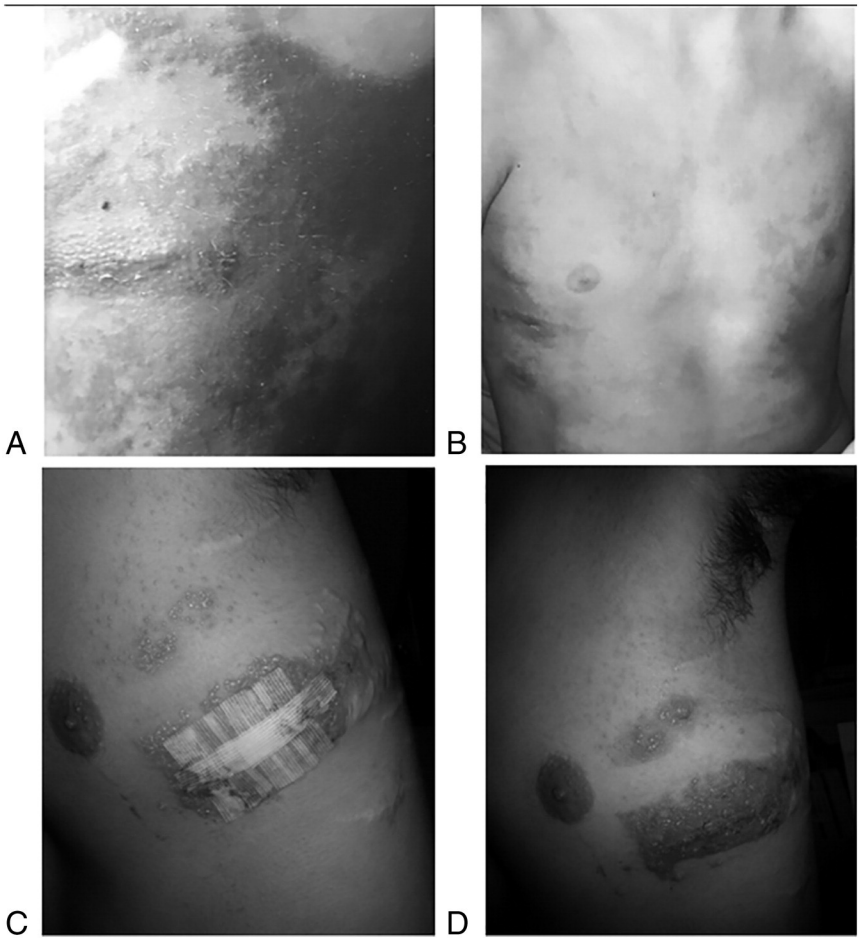

Fig. 3. Postoperative stainless steel bar allergy (A, B). Postoperative adhesive allergy (C, D).

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