Splenectomy in Elderly Patients Newly Diagnosed with Primary Immune Thrombocytopenia

Shuling Li, PhD,[1] Anne Sexter, MPH,[1] Julia T. Molony, MS,[1] Karynsa Cetin, MPH,[2] Jeffrey Wasser, MD,[3] Ivy Altomare, MD[4]

[1]Chronic Disease Research Group, Minneapolis, MN, USA; [2]Center for Observational Research, Amgen Inc., Thousand Oaks, CA, USA; [3]University of Connecticut; [4]Duke University

Introduction

- Immune thrombocytopenia (ITP) is a rare autoimmune disorder characterized by a low platelet count, which leads to increased risk of bleeding.
- Although historically a mainstay in the second-line treatment of ITP, splenectomy incidence has been declining worldwide as other medical treatments have been introduced.
- We described the current practice patterns regarding splenectomy and select outcomes in a population-based study of elderly patients newly diagnosed with ITP.

Methods

- Data source: 100% Medicare hematologic disease files (2007-2015).
- Inclusion criteria: Patients newly diagnosed with primary ITP at age ≥67 years in 2010-2014 who were continuously enrolled in Medicare Parts A and B (FFS) for 24 months before diagnosis.
  - ITP diagnosis: ≥1 inpatient or ≥2 outpatient claims at least 30 days apart but within 365 days carrying an ICD-9-CM code for ITP (287.31).
  - Date of ITP onset: date of the first ITP claim or, when applicable, the first general thrombocytopenia claim (287.3x, 287.4x, 287.5) within the 12 months before the first ITP claim.
- Exclusion criteria: Patients with secondary causes of thrombocytopenia or prior exposure to rituximab in the 12 months before the date of ITP onset.
- Baseline period: 12 months before ITP onset.
- Follow-up periods:
  - For splenectomy: from the date of ITP onset until the earlier of splenectomy or study end date (death, disenrollment from FFS coverage, or September 30, 2015).
  - For post-splenectomy events of interest: from the day after discharge until the earlier of event of interest or study end date.

Splenectomy identification:

- Claim source: ≥1 inpatient or outpatient claim carrying a billing code for splenectomy.
- Date of splenectomy: the date of service recorded on the first claim for splenectomy.

Statistical Analysis:

- Baseline characteristics at ITP onset were reported using descriptive statistics.
- Cumulative probability of splenectomy was estimated using the Kaplan-Meier method with log-rank test to assess differences by baseline characteristics.
- Bleeding and use of specific ITP therapies before and after splenectomy and adverse events of interest post-splenectomy were described using counts and percentages.

Funded by a grant from Amgen

Results

Table 1. Baseline characteristics, overall and by splenectomy status after ITP onset

Characteristics	Overall, n (%)	Splenectomy	
		Yes, n (%)	No, n (%)
Total	17,117 (100.0)	547 (100.0)	16,570 (100.0)
Age at ITP onset			
Mean(SD), years	79.1±7.6	75.9±6.2	79.2±7.7
66-69	1,919(11)	89(16)	1,830(11)
70-74	3,646(21)	174(32)	3,472(21)
75-79	3,686(22)	137(25)	3,549(21)
≥80	7,866(46)	147(27)	7,719(47)
Sex			
Male	8,475(50)	265(48)	8,210(50)
Female	8,642(50)	282(52)	8,360(50)
Race			
White	15,252(89)	510(93)	14,742(89)
African American	1,009(6)	20(4)	989(6)
Other	856(5)	17(3)	839(5)
Year of first ITP diagnosis code			
2010	4,016(24)	137(25)	3,879(23)
2011	3,652(21)	107(20)	3,545(21)
2012	3,465(20)	125(23)	3,340(20)
2013	3,122(18)	104(19)	3,018(18)
2014	2,862(17)	74(14)	2,788(17)
Select conditions at baseline[a]			
DM	5,596(33)	143(26)	5,453(33)
COPD	3,085(18)	61(11)	3,024(18)
CAD	5,573(33)	103(19)	5,470(33)
CKD	2,758(16)	47(9)	2,711(16)
CHF	3,311(19)	29(5)	3,282(20)
Any bleeding	4,160(24)	136(25)	4,024(24)
Specific bleeding			
Intracranial hemorrhage	156(1)	*	^
GI hemorrhage	1,229(7)	29(5)	1,200(7)
Hematuria	1,237(7)	35(6)	1,202(7)
Ecchymosis	367(2)	27(5)	340(2)
Epistaxis	501(3)	26(5)	475(3)

CAD, coronary artery disease; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes. GI, gastrointestinal; ITP, immune thrombocytopenia; SD, standard deviation.
*Values for cells with ten or fewer patients are suppressed.
^Values are suppressed to avoid deriving cells with ten or fewer patients.
[a]Defined in the 12 months before ITP onset.

Table 4. Select events after splenectomy among patients who were discharged alive (n=519)

Events[a]	N	%
Death	122	23.5
Pneumonia (any)	163	31.4
Deep vein thrombosis	60	11.6
Pulmonary embolism	38	7.3
Sepsis (any)	97	18.7
Bacteremia	21	4.0

[a]From the day after discharge to the end of study period.

Table 2. Cumulative probability of splenectomy after ITP onset (%)

	Time from ITP onset				
	6 months	1 year	3 years	5 years	*P* value
Overall	1.7	2.6	3.9	4.2	
Age at ITP onset, years					<.0001
66-74	2.3	3.6	5.4	5.7	
≥75	1.4	2.1	3.0	3.5	
Sex					0.6145
Male	1.6	2.5	3.8	4.2	
Female	1.8	2.7	3.9	4.3	
Race					0.0168
White	1.8	2.7	4.0	4.4	
African American	*	0.1	1.5	2.7	
Other	1.0	1.5	2.5	2.5	
Select comorbid conditions					
DM					0.0043
Yes	1.6	2.2	3.1	3.7	
No	1.8	2.8	4.2	4.5	
COPD					0.001
Yes	1.3	1.8	2.5	3.1	
No	1.8	2.8	4.1	4.5	
CAD					<.0001
Yes	1.1	1.6	2.4	2.6	
No	2.0	3.1	4.5	5.0	
CKD					0.0004
Yes	0.9	1.5	2.7	2.7	
No	1.9	2.8	4.1	4.5	
CHF					<.0001
Yes	0.4	0.9	1.3	1.3	
No	2.0	3.0	4.3	4.8	

CAD, coronary artery disease; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes; ITP, immune thrombocytopenia.

Table 3. Bleeding and use of specific ITP therapies before and after splenectomy

	Before splenectomy[a]	After splenectomy[b]
Sample size, n	547	519
Any bleeding, %	59.2	47.2
Specific bleeding, %		
Intracranial hemorrhage	3.5	3.9
Gastrointestinal hemorrhage	17.6	19..5
Hematuria	14.1	12.9
Ecchymosis	18.5	4.6
Epistaxis	12.8	10.4
Specific therapies, %		
IV Anti-D	5.7	*
IV immunoglobulins (excluding Anti-D)	46.1	17.3
IV steroids	45.3	42.2
Platelet transfusion	43.5	20.2
Rituximab	29.3	18.7

[a]From the start date of baseline period to the day before splenectomy.
[b]From the day after discharge to the end of study period.

Summary

- We identified 17,117 elderly patients with newly diagnosed ITP in 2010-2014; of these, 547 (3.2%) underwent splenectomy with a median (IQR) time to splenectomy of 6 (2-13) months.
- Overall, cumulative probability (95% confidence interval) of splenectomy at 3 years was 3.9% (3.5%-4.2%). Younger patients, white patients, and those without select comorbid conditions were more likely to undergo splenectomy than their counterparts (Table 2).
- Among splenectomized patients, at the time of splenectomy, 59% had a history of any bleeding and previous use of ITP medications was common (Table 3); post-splenectomy, 47% experienced bleeding, 31% had pneumonia, 24% died, and 19% had sepsis during a mean (SD) follow-up of 27 (19) months.

Conclusion

- Splenectomy was uncommon in elderly Medicare beneficiaries newly diagnosed with ITP, and the incidence of splenectomy was lower in older patients (age ≥75 years) and in those with select comorbid conditions.
- Post-splenectomy, the majority received a subsequent ITP medication. Bleeding and infections were common.
- Further research is needed to comprehensively examine the nature and timing of post-splenectomy outcomes among elderly ITP patients being managed in routine clinical practice.

cdrg CHRONIC DISEASE RESEARCH GROUP

www.cdrg.org