

### Emergency Department Visits Within 90 Days of Total Ankle Replacement

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### Abstract

**Background:** Total ankle replacement (TAR) utilization in the United States has steeply increased in recent decades. Emergency department (ED) visits following TAR impacts patient satisfaction and health care costs and warrant exploration. **Methods:** This retrospective cohort study utilized the 2010 to 2019 M91Ortho PearlDiver data set to identify TAR patients with at least 90 days of follow-up. PearlDiver contains billing claims data across all sites of care throughout the United States for all indications for care. Patient factors extracted included age, sex, Elixhauser Comorbidity Index (ECI), region of the country in which surgery was performed, insurance plan, and postoperative hospital length of stay. Ninety-day postoperative ED visit incidence, timing, frequency, and primary diagnoses were identified and compared to 1-year postoperative ED visit baseline data. Univariate and multivariate logistic regression analyses were used to determine risk factors for ED visits.

**Results:** Of 5930 TAR patients identified, ED visits within 90 days were noted for 497 (8.4%) patients. Of all ED visits, 32.0% occurred within 2 weeks following surgery. Multivariate analysis revealed several predictors of ED utilization: younger age (odds ratio [OR] 1.35 per decade decrease), female sex (OR 1.20), higher ECI (OR 1.32 per 2-point increase), TAR performed in the western US (OR 1.34), and Medicaid coverage (OR 2.70; 1.71-4.22 relative to Medicare) (P < .05 each). Surgical site issues comprised 78.0% of ED visits, with surgical site pain (57.0%) as the most common problem.

**Conclusion:** Of 5930 TAR patients, 8.4% returned to the ED within 90 days of surgery, with predisposing demographic factors identified. The highest incidence of ED visits was in the first 2 postoperative weeks, and surgical site pain was the most common reason. Pain management pathways following TAR should be able to be adjusted to minimize the occurrence of postoperative ED visits, thereby improving patient experiences and decreasing health care utilization/costs.

Level of Evidence: Level III, retrospective cohort study.

Keywords: ankle, total ankle replacement, total ankle replacement, emergency department, risk factors, timing

### Introduction

Postoperative readmissions are a commonly used metric of quality of orthopaedic care and an important target for quality improvement and cost reduction because of their substantial burden on patients and health care systems.<sup>6,17,38,40,47</sup> Despite a drastic increase in the number of total ankle replacement (TAR) performed in the United States over the past few decades, postoperative emergency department (ED) visits after TAR have not been adequately investigated.<sup>8,10,15,19,44</sup>

ED visits following surgery have negative implications for both patients and hospitals as they are associated with poorer patient satisfaction and high cost.<sup>8,10,15,19,44</sup> ED visit may indicate inadequate coordination of postoperative care. Identifying and addressing related issues could be useful for quality improvement programs.<sup>15</sup> Further, with annual costs of potentially avoidable ED visits estimated at close to \$65 billion, there remains much room for improvement.<sup>8</sup>

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Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (https://creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage). Studies have examined ED visits following elective foot and ankle procedures and open reduction and internal fixation (ORIF) for treatment of ankle fracture.<sup>2,31,39</sup> These studies report that postoperative ED visits are common, with 30-day incidences ranging from 7% to 22%. However, cohort sizes have been limited to less than 600 patients. Moreover, mixed foot and ankle surgeries were analyzed together.

As the Centers for Medicare & Medicaid Services expands value-based payment systems to include 90-day outcomes in reimbursement considerations, examining ED visits in larger, nationwide populations undergoing specific procedures is becoming increasingly important.<sup>24,27</sup> The current study used a large national administrative database composed of billing claims data across all sites of care in the United States to identify a sizable cohort of patients with TAR and describe the incidence, predictive factors, and reasons for 90-day postoperative ED visits.

### Methods

### Database and Cohort

All data used in the present study was identified via PearlDiver Technologies. PearlDiver contains more than 41 billion patient billings claims records collected across all sites of care throughout the United States. The PearlDiver database contains information across all medical specialties and originates all provider types, including facility, physician, and pharmacy. For this retrospective cohort study, data were abstracted from the 2010 to 2019 PearlDiver M91Ortho data set. The M91Ortho data set constitutes a subset over the overall PearlDiver database and contains deidentified billing claims information-in line with the Health Insurance Portability and Accountability Act (HIPAA)-on approximately 91 million orthopaedic patients in the United States. Given the aggregated and deidentified nature of PearlDiver data, our institutional review board (IRB) granted all studies utilizing this data set exemption from review.

Patients who underwent TAR were identified by *Current Procedural Terminology* (*CPT*) code 27702 (total ankle reconstruction with implant). Patients not followed by the data set for at least 90 days following the procedure were excluded. Patients were extracted and characteristics tabulated, including age, sex, Elixhauser Comorbidity Index (ECI, a patient comorbidity index constructed via ICD diagnosis codes), region of the country according to US Census Bureau definitions (West, South, Midwest, Northeast), insurance plan (commercial, Medicaid, Medicare), and postoperative hospital length of stay ( $\geq 1$  night(s), sameday discharge). The quantitative variables age and ECI were grouped by decade and per 2-point increase, respectively, based on the PearlDiver output and to facilitate ease of analysis and interpretation.

### Emergency Department Visits and Readmissions

Postoperative ED visit within the 90 days following TAR were identified based on the usage of ED visit *CPT* codes: *CPT*-99281, *CPT*-99282, *CPT*-99283, *CPT*-99284, and *CPT*-99285. Total number of ED visits and ED visits per week were determined from this data. A baseline for weekly ED visits was determined for study cohort by averaging the incidence of ED visits in weeks 52-56 following TAR. For this calculation, patients were excluded if they were not followed in the database for a minimum of 56 weeks following surgery.

International Classification of Diseases (ICD) codes listed as patients' primary diagnosis for ED visits were used to determine reasons for ED visits. Using PearlDiver, a list of *ICD* codes as well as the number of patients listed under each code for primary diagnosis for an ED visit following TAR was determined. Supplemental Table 1 depicts the ED visit ICD primary diagnosis codes among patients who visited the ED following TAR.

Based on the *ICD* codes identified, the postoperative ED visits were manually grouped and categorized as pain, surgical site infection, venous thromboembolism (VTE), cardiovascular, gastrointestinal, and respiratory. These categories were further divided as being related to the surgical site (pain, infection, and VTE) vs unrelated to the surgical site (cardiovascular, gastrointestinal, and respiratory).

### Data Analysis

Univariate analysis was conducted to compare characteristics of TAR patients who did and did not utilize the ED following surgery. Differences in sex, region, insurance plan, and postoperative hospital length of stay between patients in the 2 groups were compared via Pearson  $\chi^2$  test. Welch *t* test was used to compare average age and ECI of patients in the 2 groups. Multivariate logistic regression was then used to determine factors independently associated with ED utilization and odds ratios were calculated for each factor analyzed compared with referent categories. This method of analysis helped to reduce any potential confounding bias. Statistical analysis was conducted within the PearlDiver system—with statistical significance designed as P < .05. Prim9 (GraphPad Software, San Diego, CA) and Microsoft Excel (Microsoft Corporation, Redmond, WA) were used to create all figures.

### Results

### Study Cohort and Incidence of ED Visits

A total of 6238 TAR patients were identified. Of this population, 308 (4.93%) were excluded because of <90-day postoperative follow-up data in the PearlDiver database. The final study cohort was thus 5930 TAR patients, of whom 90-day postoperative ED visits were noted for 497 (8.4%) patients (Figure 1).

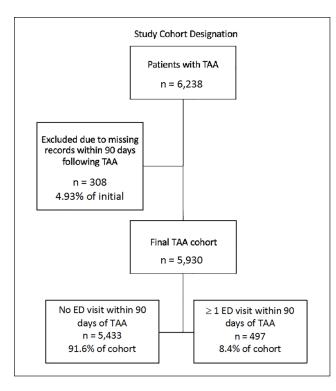


Figure 1. Flow chart depicting separation of study cohorts.

The overall occurrence of such ED visits and their weekly distribution are shown in Figure 2. Among patients who presented to the ED within 90 days of total ankle replacement, 1 ED visit was reported for 397 patients, 2 ED visits for 73 patients, 3 ED visits for 12 patients, and  $\geq$ 4 ED visits for 15 patients.

Of all ED visits within 90 days following TAR, 32% occurred within the first 2 weeks. In the first week following TAR, 140 patients (2.36% of the study cohort) visited the ED, followed by 69 patients (1.16%) during the second week. By week 3 following TAR, the number of patients visiting the ED decreased to 0.73% (43 patients) and approximately plateaued thereafter.

Compared with the 8.4% of patients who visited the ED within the 90 days following TAR, readmissions were identified for 244 patients (4.11% of the study population and 49.1% of the number who had presented to the ED).

## Factors Associated With Postoperative ED Utilization

Patient characteristics of the entire TAR study population are shown in Table 1. The overall 5930 TAR patients had an average  $\pm$  SD age of 62.5  $\pm$  10.3 years, with females representing 49.5%. As measured by ECI, the study cohort had, on average, a moderate to high number of comorbidities (average ECI 3.9  $\pm$  3.0). Patients were more likely to have their TAR procedure performed in the midwestern and southern United States (31.4% and 31.8%, respectively), compared with the northeast or west (16.4% and 20.2%, respectively). Most patients in the study cohort had commercial insurance (72.4%). The majority of patients in the study cohort had a postoperative hospital length of stay greater than or equal to 1 night (60.1%) as opposed to same-day discharge (39.9%).

Patient characteristics were then defined for those that did not and did visit the ED within the 90 days following surgery (Table 1). Univariate analysis revealed that all demographic variables analyzed—other than region of the country in which surgery was performed (P = .3744)—were significantly correlated with patients visiting the ED within 90 days following TAR (P < .0001 for age, sex, ECI, and insurance; P = .0425 for postoperative length of stay).

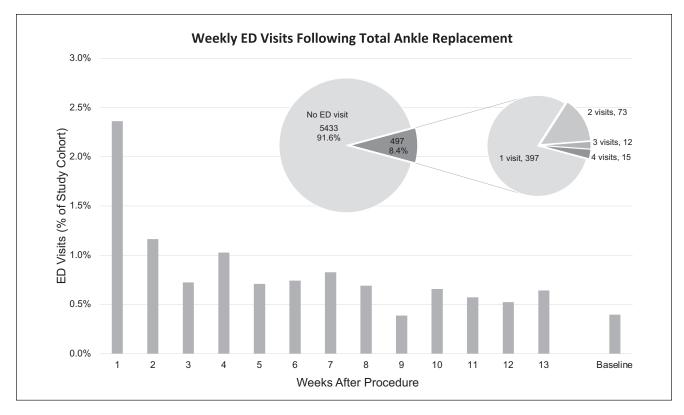
The results of multivariate logistic regression are listed in Table 2 and visually depicted in Figure 3. After separating patients by age (grouped by decade: <20, 20-29, 30-39, 40-49, 50-59,  $\geq$ 59), ED visits within 90 days of TAR were independently associated with younger age (per decade decrease, odds ratio [OR] 1.35, 95% CI 1.23-1.48). ED visits within 90 days of TAR were also independently associated with higher ECI (ie, increasing comorbidity burden) (per 2-point increase: OR 1.32, 95% CI 1.25-1.40), having TAR performed in the Western United States (OR 1.34, 95% CI 1.03-1.76), and patient insurance plan (compared with Medicare, Medicaid [OR 2.70, 95% CI 1.71-4.22]). ED visits within 90 days of TAR were not associated with patient sex (compared to male, female [OR 1.20, 95% CI 0.99-1.46]) or postoperative hospital length of stay (compared to  $\geq 1$  night length of stay, same-day discharge [OR 1.14, 95% CI 0.94-1.39]).

### Reasons for Postoperative ED Utilization

Reasons for visit to the ED within the 90 days following TAR are shown in Figure 4. These included postoperative pain (57.0% of those visiting the ED), surgical site infection (13.0%), VTE (8.52%), and cardiovascular (11.2%), respiratory (5.38%), and gastrointestinal disorders (4.93%). Postoperative pain, surgical site infection, and VTE were grouped as diagnoses "related to surgical site," making up 78.5% of the primary ED visit diagnoses. In contrast, diagnoses not related to the surgical site (cardiovascular, respiratory, and gastrointestinal disorders) accounted for just 21.5% of primary ED visit diagnoses.

### Discussion

Short- and longer-term outcomes of TAR have been reported.<sup>1,3,16,18,21,25,46</sup> Overall, TAR has been shown to be a safe procedure, with good long-term outcomes.<sup>5</sup> However, the current study demonstrates that 8.4% of a large cohort of patients undergoing TAR visited the ED at least once



**Figure 2.** Bar graph depicts weekly incidence of ED visits following total ankle replacement. Pie chart shows breakdown of patients who visited vs did not visit the ED following surgery. The baseline for weekly ED visit incidence was calculated by averaging weekly visits between 52 and 56 weeks following total ankle replacement. ED, emergency department.

	Total (N = 5930; 100%)	No ED Visit (n = 5433; 91.6%)	ED Visit (n = 497; 8.4%)	P Value
Age, y (mean ± SD)	62.48 ± 10.3	62.78 ± 10.0	59.3 ± 12.4	
<20	<10	<10	<10	<.0001
20-29	33 (0.6)	16 (0.3)	<10	
30-39	126 (2.1)	104 (1.9)	16 (3.2)	
40-49	438 (7.4)	364 (6.7)	72 (14.5)	
50-59	1506 (25.4)	1379 (25.4)	126 (25.4)	
60-69	2420 (40.8)	2263 (41.7)	149 (30.0)	
>70	1447 (24.4)	1339 (24.6)	109 (21.9)	
Sex				
Female	2933 (49.5)	2645 (48.7)	288 (57.9)	<.0001
Male	2997 (50.5)	2788 (51.3)	209 (42.1)	
ECI (mean $\pm$ SD)	3.9 ± 3.0	3.78 ± 2.96	5.58 ± 3.6	
0-1	1321 (22.3)	1265 (23.3)	44 (8.9)	<.0001
2-3	1841 (31)	1699 (31.3)	125 (25.2)	
4-5	1295 (21.8)	1190 (21.9)	111 (22.3)	
>5	1473 (24.8)	1279 (23.5)	217 (43.7)	
Region				
Midwest	1862 (31.4)	1700 (31.3)	163 (32.8)	.3744
Northeast	971 (16.4)	884 (16.3)	87 (17.5)	
South	1884 (31.8)	1746 (32.1)	138 (27.8)	
West	1197 (20.2)	1088 (20)	108 (21.7)	

Table 1. Univariate Analysis of Characteristics of Patients With Total Ankle Replacement Surgery.<sup>a</sup>

(continued)

### Table I. (continued)

	Total (N = 5930; 100%)	No ED Visit (n = 5433; 91.6%)	ED Visit (n = 497; 8.4%)	P Value
Insurance				
Commercial	4292 (72.4)	3921 (72.2)	370 (74.4)	<.0001
Medicaid	201 (3.4)	156 (2.9)	45 (9.1)	
Medicare	1407 (23.7)	1327 (24.4)	80 (16.1)	
Postoperative length of stay				
$\geq$ I night(s)	3564 (60.1)	3287 (60.5)	277 (55.7)	.0425
Same-day discharge	2366 (39.9)	2146 (39.5)	220 (44.3)	

Abbreviations: ECI, Elixhauser Comorbidity Index; ED, emergency department.

<sup>a</sup>P values significant at <.05 (boldface indicates significance). Unless otherwise noted, values are n (%). Percentages are what proportion of patients within a cohort (total, no ED visit, ED visit) have a particular demographic factor (ie, % of total patients who are female is 2933/5930  $\times$  100 = 49.5%.

**Table 2.** Multivariate Analysis of Predictive Factors for ED Utilization (N = 5930).

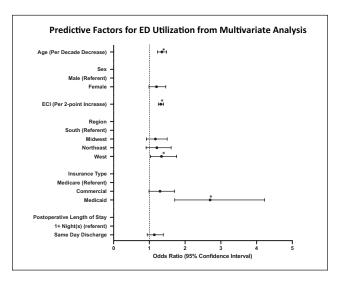
	OR (95% CI)	P Value <sup>a</sup>
Age (per decade decrease)	1.35 (1.48, 1.23)	<.0001
Sex		
Male (referent)		
Female	1.2 (0.99, 1.46)	.063
ECI (per 2-point increase)	1.32 (1.25, 1.4)	<.0001
Region		
South (referent)		
Midwest	1.17 (0.92, 1.5)	.1913
Northeast	1.21 (0.91, 1.61)	.1835
West	1.34 (1.03, 1.76)	.0312
Insurance		
Medicare (referent)		
Commercial	1.3 (0.99, 1.71)	.059
Medicaid	2.7 (1.71, 4.22)	<.0001
Postoperative length of stay		
$\geq$ I night(s) (referent)		
Same-day discharge	1.14 (0.94, 1.39)	.1775

Abbreviations: ECI, Elixhauser Comorbidity Index; ED, emergency department; OR, odds ratio.

<sup>a</sup>P values were significant at <.05 (boldface indicates significance).

during the 90-day postoperative period, with almost a quarter of those visiting the ED more than once. Rates of 90-day postoperative ED utilization are similar in other orthopaedic procedures, including 11.8% following total hip and knee arthroplasty,<sup>30</sup> 8.3% following anterior cruciate ligament reconstruction,<sup>13</sup> and 11.9% following single-level anterior cervical discectomy and fusion.<sup>12</sup>

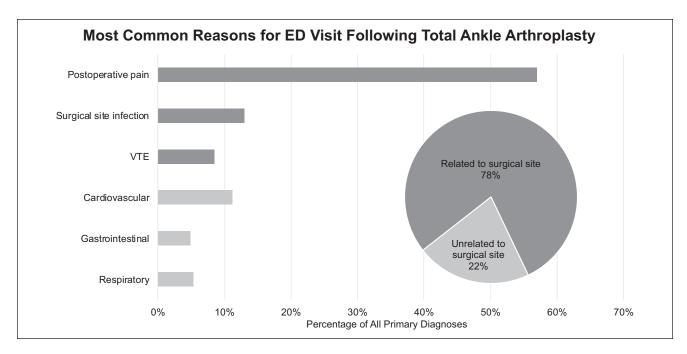
In terms of timing of post-TAR ED visits, 32.0% occurred within the first 2 weeks, constituting the greatest density of visits within the 13-week study period. This indicates that the first 2 weeks following surgery are the most important to focus on from a care pathway perspective. Further, the substantial percentage of patients who visited



**Figure 3.** Forest plot depicting results of multivariate analysis for independent predictive factors for ED utilization within 90 days of total ankle replacement surgery. Error bars represent 95% Cls. Asterisks indicate statistical significance (P < .05).

the ED more than once (100/497, 20.1%) suggests that there is a specific subpopulation that needs special attention. Multivariate analysis identified independent predictors of such ED visits to help target the evolution of care mitigation strategies. Overall, younger age, increased ECI, West geographic region, and Medicaid insurance were found to be positive predictors of postoperative ED visits, but patient sex and postoperative hospital length of stay were not.

Younger patients (per decade decrease, after stratifying patients into age groups <20, 20-29, 30-39, 40-49, 50-59, 59+) were found to have a 1.35 higher odd of visiting the ED during the postoperative period. Although intuitively, one might expect older patients to utilize the ED more, prior studies have described greater ED utilization among younger patients following total hip and knee arthroplasty, anterior crucial ligament reconstruction, and ankle fracture



**Figure 4.** Most frequent primary diagnosis among total ankle replacement patients who visited the ED within 90 days of surgery divided by relation to the surgical site.

surgery as compared to older patients.<sup>7,13,31</sup> This is potentially due to the greater effect of pain in younger patient populations. Additionally, the increased comorbidity burden of older patients was accounted for with the multivariate nature of the analyses performed.

Patients with a higher comorbidity burden were more likely to present to the ED (1.32 per 2-point increase in ECI). Logically, this relationship makes sense as patients with higher comorbidity burdens are at greater risk of more complications.<sup>22,33</sup> Notably, a study published by Cunningham et al in 2018 analyzed 1024 TAR patients from a single center (less than a fifth of the current study population) and found that patient's comorbidities did not influence ED visitation within 90 days following surgery.<sup>4</sup> The present study demonstrates contradicting results, showing that patient comorbidities did play a major role in ED utilization—possibly explained by greater statistical power.

Geographic region of the county where the procedure was performed influenced the likelihood of visiting the ED following TAR (odds ratio highest in the West, with odds of 1.34 relative to the South). This may represent different overall ED utilization parameters in different parts of the country. Other studies evaluating postoperative ED visits have also found regional variation in ED utilization.<sup>13,20</sup>

In terms of insurance coverage, patients with Medicaid insurance were more than  $2\frac{1}{2}$  times more likely to utilize the ED (odds ratio 2.70), the largest predictor if a patient would utilize the ED. Although it is not entirely clear what factors specifically lead to Medicaid patients visiting the ED, this finding is in line with previous literature demonstrating a similar association.<sup>32,41,42</sup> It is possible that Medicaid patients exhibit the highest postoperative ED utilization secondary to more limited access to non-ED venues of care. Additionally, Medicaid patients may be incentivized to seek postoperative care in the ED because of copay exemption.

In terms of reason for presenting to the ED following TAR, most were related to the surgical site (78.5% of postoperative ED visit). Previous studies have found that the majority of ED visits following other orthopaedic procedures such as total hip and knee arthroplasty are related to the index surgery.<sup>26</sup> Of these cases, postoperative pain was the most common complaint, consistent with findings seen following other orthopaedic surgeries.13,32 Specifically, previous studies examining ED utilization following total hip and knee arthroplasty have reported postoperative pain as the largest individual reason for patient presentation.<sup>26</sup> This suggests better pain regimens and/or education is needed prior to discharge. For one, perioperative pain management counseling with personalized pain control regimens based on risk assessment have been shown to reduce patient perceived pain intensity and required opioid doses while increasing patient well-being and satisfaction.<sup>28,37</sup> Furthermore, nurse navigators with an expertise in pain management may be involved in the postoperative care pathway, helping patients better cope with postoperative pain and thereby reducing the need for pain-related ED utilization.<sup>34</sup> Additionally, check-in visits with surgeons in the first weeks following TAR may reduce patient reliance on the ED for postoperative pain management.

The next most common surgical site reason for visiting the ED postoperatively was surgical site infection-making up approximately 1.1% of the total study cohort. Surgical site infection is a common reason for readmission following surgery,<sup>14,23,29,43</sup> and thus is an important metric. Following surgical site infection, the next most common surgical siterelated ED diagnosis was VTE, occurring in 0.72% of total TAR cohort. Previous studies have found VTE to be a relatively uncommon, but nonetheless important postoperative complication of TAR and other foot and ankle surgery.<sup>11,36,45</sup> Postoperative care pathways may require modification to reduce the risk of VTE, including enhanced pharmacologic prophylaxis<sup>35</sup> as well as encouraging patient mobility and rehabilitation.<sup>9</sup> Such measures have been shown to reduce the risk of VTE following orthopaedic procedures. Nonsurgical site reasons for presenting to the ED postoperatively, such as cardiovascular, gastrointestinal, or respiratory, each made up a small percentage of the ED visits. These factors must be kept in mind, but together represented only 24% of the reasons for postoperative ED visits.

The present study has several limitations. With any study that makes use of administrative data, it is reliant and thus limited to the accuracy of the administrative data that was coded. Furthermore, CPT-27702, which was used to identify patients who underwent TAR, can be coded for patients undergoing revision surgery. Revision surgery is recognized to involve greater complexity and complications. Given this, a small fraction of the present study's cohort may have undergone revision surgery, which may have had a marginal impact on the rate of postoperative ED utilization. Additionally, there can be a multitude of reasons an individual may visit the ED following a surgery; however, our data only present what was recorded as their primary concern and can only infer an attribution to the index TAR. Moreover, there remains the possibility of misclassification of postoperative complications based on ICD coding. Lastly, it is important to note that any causal inference that TAR leads to higher than baseline rates of postoperative ED utilization is prone to unobserved confounding factors.

### Conclusions

Overall, of 5930 TAR patients, 8.4% returned to the ED within 90 days of surgery, with predisposing demographic factors identified. The highest incidence for these ED visits was in the first 2 postoperative weeks, and surgical site pain was the most common reason. Given the large national sample used to conduct this study, it is presumable that results will translate to the total TAR population in the United States. Care pathways—particularly those related to pain management—should be able to be adjusted to minimize the occurrence of ED utilization following TAR. More specifically, pre- and postoperative pain management counseling, pain management nurse navigators, and more frequent

early postoperative check-in visits with surgeons may help patients better manage postoperative pain, thereby reducing ED utilization, improving patient experiences, and minimizing health care utilization and costs.

### Ethical Approval

Ethical approval for this study was waived by the Yale Institutional Review Board because it determined that the investigator is not engaged in research involving human subjects.

### **Declaration of Conflicting Interests**

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Philip P. Ratnasamy, BS, reports grants or contracts from the National Institutes of Health (Award 2T35HL007649-36). ICMJE forms for all authors are available online.

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Diagnosis Category	ICD Diagnosis Code	Description	
Postoperative Pain	ICD-10-D-G8918	Other acute postprocedural pain	
	ICD-9-D-71947	Pain in joint ankle and foot	
	ICD-10-D-M25571	Pain in right ankle and joints of right foot	
	ICD-10-D-M25572	Pain in left ankle and joints of left foot	
	ICD-9-D-33818	Other acute postoperative pain	
	ICD-9-D-7295	Pain in limb	
VTE	ICD-10-D-12699	Other pulmonary embolism without acute cor pulmonale	
	ICD-10-D-1743	Embolism and thrombosis of arteries of the lower extremities	
	ICD-10-D-182411	Acute embolism and thrombosis of right femoral vein	
	ICD-10-D-182451	Acute embolism and thrombosis of right peroneal vein	
	ICD-10-D-182621	Acute embolism and thrombosis of deep veins of right upper extremity	
	ICD-9-D-41519	Other pulmomary embolism and infarction	
	ICD-9-D-45340	Acute embolism and thrombosis of unspecified deep veins of unspecified lower extremity	
Surgical Site Infection	ICD-10-D-L03115	Cellulitis of right lower limb	
	ICD-9-D-99859	Other postoperative infection	
Cardiovascular	ICD-9-D-78659	Other chest pain	
	ICD-9-D-78650	Chest pain unspecified	
Respiratory	ICD-10-D-R0602	Shortness of breath	
Gastrointestinal	ICD- 10-D-K5900	Constipation unspecified	

**Supplemental Table I.** International Classifications of Disease Codes and Descriptions From Primary Diagnoses During Emergency Department Visits Manually Grouped Into Categories of Reasons for Emergency Department Utilization.

Abbreviations: ICD, International Classification of Diseases; VTE, venous thromboembolism.