Current trends in preoperative biliary stenting in patients with pancreatic cancer

Lindsay J. Jinkins, BA,[a] Abhishek D. Parmar, MD,[a,b] Yimei Han, MS,[a] Casey B. Duncan, MD, MS,[a] Kristin M. Sheffield, PhD,[a] Kimberly M. Brown, MD,[a] *and* **Taylor S. Riall, MD, PhD,[a]** *Galveston, TX, and Oakland, CA*

Background. *Sufficient evidence suggests that preoperative biliary stenting is associated with increased complication rates after pancreaticoduodenectomy.*
Methods. *Surveillance, Epidemiology, and End Results (SEER) and linked Medicare claims data (1992–2007) were used to identify patients with pancreatic cancer who underwent pancreaticoduodenectomy. We evaluated trends in the use of preoperative biliary stenting, timing of physician visits relative to stenting, and time to surgical resection and symptoms in stented and unstented patients.*
Results. *Pancreaticoduodenectomy was performed in 2,573 patients, and 52.6% of patients underwent preoperative biliary stenting (*N = *1,354). Of these, 75.3% underwent endoscopic stenting only, 18.9% received a percutaneous stent, and 5.8% underwent both procedures. The overall stenting rate increased from 29.6% of patients between 1992 and 1995 to 59.1% between 2004 and 2007 (*P < *.0001). Preoperative stenting was more common in patients with jaundice, cholangitis, pruritus, or coagulopathy (*P < *.05 for all). Of stented patients, 77.7% had had a stent placed prior to seeing a surgeon. Stenting prior to surgical consultation was associated with longer indwelling stent time compared to stenting after surgical consultation (37.3 vs 27.0 days,* P < *.0001). In addition, stented patients had longer times from surgeon visit to pancreatectomy than those who had not received stents (24.2 days vs 17.2 days,* P < *.0001).*
Conclusion. *Use of preoperative biliary stenting doubled between 1992 and 2007 despite evidence that stenting is associated with increased perioperative infectious complications. The majority of stenting occurred prior to surgical consultation and is associated with significant delay in time to operation. Surgeons should be involved early in order to prevent unnecessary stenting and improve outcomes. (Surgery 2013;154:179-89.)*

From the Department of Surgery,[a] The University of Texas Medical Branch, Galveston, TX; and the Department of Surgery,[b] The University of California, San Francisco-East Bay, Oakland, CA

Preoperative biliary stenting was introduced in the 1960s and 1970s in an effort to improve surgical outcomes in patients with pancreatic cancer undergoing curative-intent resection. This was done to correct physiologic disturbances induced by hyperbilirubinemia secondary to malignant obstruction, theoretically optimizing patients' conditions prior to operation and improving perioperative morbidity and mortality. Early retrospective studies[1-4] and small prospective randomized trials[5-8] yielded mixed results, some finding benefit[1-3,5] with stenting and others finding no benefit.[4,6-8]

The theoretical benefits of preoperative biliary stenting have not been demonstrated consistently in practice. Large retrospective analyses comparing stented to unstented patients report either no significant differences in surgical outcome[9-12] or increased rates of infectious complications with preoperative biliary stenting.[13-17] Several meta-analyses in the past decade corroborated these findings and recommended against the routine use of preoperative biliary stenting in patients undergoing pancreaticoduodenectomy.[18-21] A recent prospective randomized trial reported a significantly increased overall complication rate

Supported by grants from the National Institutes of Health (1K07CA130983-01A1, UL1TR000071 and T32 DK007639) and the Cancer Prevention Research Institute of Texas (grant # #RP101207-P03).

Accepted for publication March 28, 2013.

Reprint requests: Taylor S. Riall, MD, PhD, Department of Surgery, University of Texas Medical Branch, 301 University Boulevard, Galveston, TX 77555-0541. E-mail: tsriall@utmb.edu.

0039-6060/$ - see front matter

http://dx.doi.org/10.1016/j.surg.2013.03.016

in stented patients compared to those who proceeded directly to surgery, and many of the reported complications were related to the stenting procedure itself.[22]

In the setting of this evolving literature, we used the Surveillance, Epidemiology, and End Results (SEER) tumor registry and linked Medicare-claims data to examine trends in the use of preoperative biliary stenting between 1992 and 2007. In addition, we evaluated factors that were associated with the receipt of preoperative biliary stenting. Based on clinical experience, we hypothesized that preoperative biliary stenting had not decreased over this period and that the majority of stenting occurred prior to surgical consultation and evaluation.

METHODS

This study was approved by the Institutional Review Board at the University of Texas Medical Branch.

Data source. We used data from the National Cancer Institute's SEER tumor registry and linked Medicare-claims data collected by the Center for Medicare and Medicaid Services. Developed by the National Cancer Institute, the SEER program collects information about cancer incidence and survival from population-based cancer registries that currently cover approximately 28% of the US population.[23] SEER provides information on patients' demographics, primary tumor site, histology, stage of disease, first course of treatment, and survival status.

The Medicare data include all claims for covered health care services, including inpatient and outpatient care, for all Medicare patients. The study included patients aged 66 years and older who were diagnosed between 1992 and 2007 and their Medicare claims through 2009.[24]

Cohort selection. Our cohort selection is summarized in Fig 1. The cohort included patients with a primary diagnosis of adenocarcinoma of the pancreas between 1992 and 2007. *International Classification of Disease for Oncology*, 3rd edition (ICD-O-3) morphology codes were used for adenocarcinoma (8000/3, 8010/3, 8020/3, 8021/3, 8022/3, 8140/3, 8141/3, 8211/3, 8230/3, 8500/3, 8521/3, 8050/3, 8260/3, 8441/3, 8450/3, 8453/3, 8470/3, 8471/3, 8472/3, 8473/3, 8480/3, 8481/3, 8503/3). All International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) and American Medical Association Common Procedure Terminology (CPT) codes used for the analysis are

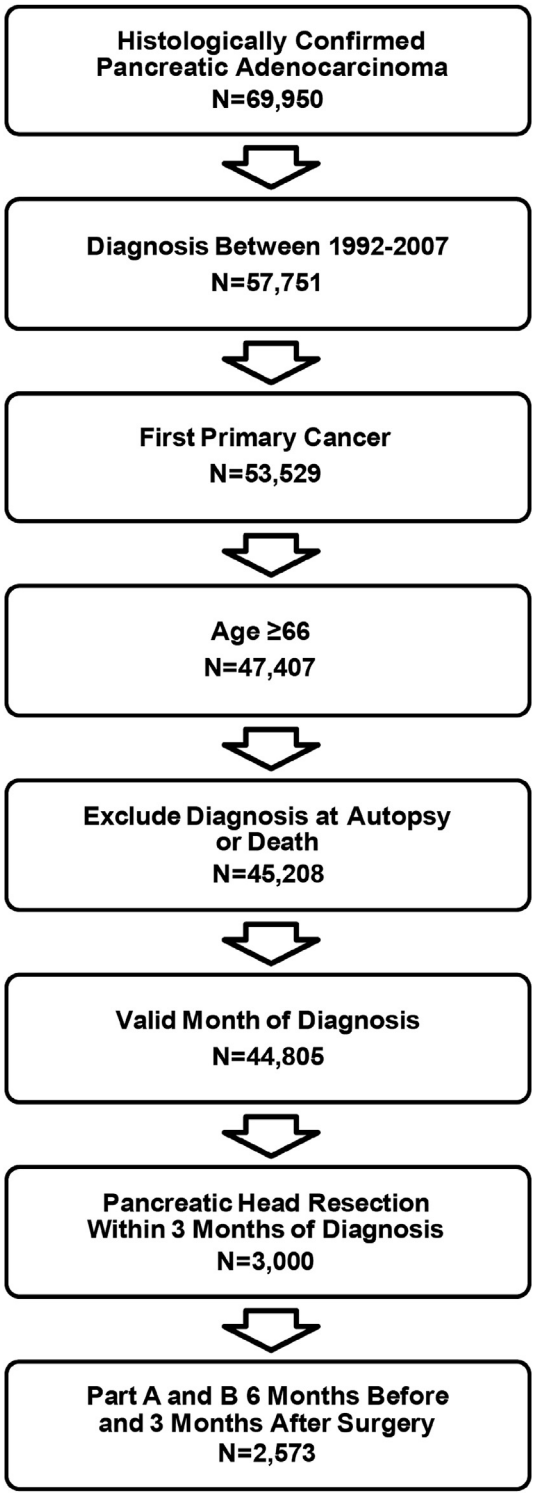

Fig 1. Cohort selection. We included all patients with a primary diagnosis of pancreatic adenocarcinoma between 1992 and 2007. Only patients 66 years and older with histologically confirmed and surgically resected adenocarcinoma within 3 months of diagnosis were included. Patients were excluded if they did not have Medicare Part A and B without an HMO for 6 months before and 3 months after surgery.

Table I. ICD-9-CM and CPT codes for preoperative procedures, surgeon visits, and symptoms

	ICD-9 codes	*CPT/HCPCS codes*
Procedures		
Pancreatic head resection	52.6, 52.7, 52.51	48150, 48152, 48153, 48154, 48155
ERCP	51.10, 51.11, 51.84-51.87, 51.99, 52.13, 52.93	74328-74330, 43260-43269, 43271, 43272
With endostent	51.86, 51.87, 51.99	43267-43269
Without endostent	51.10, 51.11, 51.84, 51.85, 52.13, 52.93	74328-74330, 43260-43266, 43271, 43272
PTC/drain	51.98, 87.51	74320
Chemotherapy*	ICD-9 diagnosis codes: V58.1, V66.2, V67.2 ICD-9 procedure codes: 99.25 DRG code: 410	HCPCS/CPT codes: 96400-96549, Q0083, Q0084, Q0085, J7150, J2353, J2354, J9000-J9999 Revenue center codes: 0331, 0332, 0335
CT abdomen	88.01	74150, 74160, 74170, 74175, 76376, 76377
MRI abdomen	88.97	74181, 74182, 74183, 74185
EUS	NA	76975, 43231, 43232, 43259
Surgeon visits		
Outpatient evaluation and management	NA	99201-99205, 99211-99215, 99241-99245
Inpatient evaluation and management	NA	99221-99223, 99231-99236, 99238, 99251-99255
Symptoms		
Jaundice	782.4	NA
Cholangitis	576.1	NA
Pruritis	698.9	NA
Coagulopathy	286.7	NA

*Neoadjuvant therapy is defined as chemotherapy during the 6 months prior to surgical resection.
CT, Computed tomography; *ERCP*, endoscopic retrograde cholangiopancreatography; *EUS*, endoscopic ultrasound; *MRI*, magnetic resonance imaging; *NA*, not applicable; *PTC*, percutaneous transhepatic cholangiogram.

shown in Table I. We included beneficiaries aged 66 years and older who underwent pancreatic head resection within 3 months of diagnosis (Fig 1) and were enrolled in Medicare Part A and Part B without HMO for 6 months before and 3 months after surgery or until death. We excluded patients in whom pancreatic cancer was not the first primary and in whom the diagnosis was made at autopsy or by death certificate only.

Measures. Endoscopic and percutaneous stenting were identified by using both ICD-9 procedure codes and CPT codes in the carrier, Medicare Part A inpatient billing claims, and outpatient standard analytic file (Table I). These codes included both insertion and replacement of stents or percutaneous biliary drains and excluded isolated pancreatic duct stenting. Dates of stenting procedures were obtained from Medicare claims, with the date of the first procedure used if multiple stenting procedures were performed. ICD-9 and CPT codes for endoscopic retrograde cholangiopancreatography (ERCP) without stenting (Table I) were not included but were used to determine presumed failed endostenting if they occurred prior to or on the same day as percutaneous stenting. We also identified newer technologies such as computed tomography (CT), magnetic resonance imagery (MRI), and endoscopic ultrasound (EUS) in carrier and outpatient standard analytic files with the following codes (CT abdomen: ICD-9: 88.01, CPT: 74150, 74160, 74170, 74175, 76376, 76377; MRI abdomen: ICD 9: 88.97, CPT: 74181, 74182, 74183, 74185, EUS: CPT: 76975, 43231, 43232, 43259).

Patients were classified as having: (1) localized disease (AJCC 0, IA, IB); (2) regional disease (AJCC IIA, IIB, III); or (3) distant disease (AJCC IV) using the SEER historic stage.[25] The SEER historic stage is based on the best available data, using a combination of pathologic observations, intraoperative observations, and clinical observations, in this order of priority. Neoadjuvant therapy was defined as receipt of chemotherapy (Table I) in the 6 months prior to surgical resection.

The date of surgery was determined from the associated Medicare claim. To identify the first visit to a surgeon, we used the carrier files to identify evaluation and management codes for office or other outpatient services and consultations and

hospital inpatient services and consultations (Table I). The Medicare Health Care Financing Administration specialty claims code associated with the claim was identified. Surgeon specialty was defined by Medicare specialty codes 02 (general surgery) and 91 (surgical oncology). The date of the first visit to a surgeon was defined as the date of the first visit to a surgeon before the date of surgical resection or the date of surgical resection if there was no prior documented surgeon visit. We identified the first gastroenterologist visit by using evaluation and management claims for gastroenterologist (Medicare specialty code 10). The first visit was considered the date of first evaluation and management code or the first endostent/ERCP code, whichever was earlier.

Demographic variables included age, gender, race, marital status, SEER region, quartiles of education, and median income. SEER-Medicare does not provide patient-level information for education and income, so patients were placed into education and income quartiles based on zip-code-level data. Zip-code-level data were obtained from the 2000 census and included median income and the percentage of residents with fewer than 12 years of education. Quartile 1 is the least educated (highest percentage without high school education) or lowest income quartile, and quartile 4 is the highest. Symptoms in the 3 months prior to surgery were identified using ICD-9 codes of inpatient or outpatient claims, including jaundice (782.4), cholangitis (576.1), pruritus (698.9), and coagulopathy (286.7).

Statistical analysis. Summary statistics were calculated for the entire cohort. We calculated the overall proportion of patients undergoing preoperative endoscopic or percutaneous stenting procedures. These were not mutually exclusive. Therefore, stented patients were classified as having undergone endoscopic procedures, percutaneous procedures, or both. In patients who underwent both endostenting and percutaneous stenting, we evaluated the relative timing of the 2 procedures. We also evaluated the timing of stent placement relative to surgical evaluation. Among stented patients, the proportion stented prior to seeing a surgeon was examined as were time trends in the rate of stenting prior to seeing a surgeon.

Time trends in the use of stenting procedures (overall, endoscopic, and percutaneous) during the study period were examined using the Cochran-Armitage test for trend. Time trend analyses were performed using all SEER regions and then repeated, excluding New Jersey, greater California, Kentucky, and Los Angeles, which were added in 2001 (first full year of data, 2000). Because the results were identical, we report the results for the entire cohort.

We also evaluated the timing of stent placement relative to surgical evaluation. Among stented patients, the proportion stented prior to seeing a surgeon was examined as were time trends in the rate of stenting prior to seeing a surgeon.

The Student t test was used to compare time from surgical visit to surgical resection in stented and unstented patients and time from stenting to surgical resection in patients stented before and after seeing a surgeon. The proportion of patients who were stented within 1 week and 2 weeks of surgery was calculated.

The frequency of symptoms in the 3 months prior to surgery (jaundice, cholangitis, pruritus, coagulopathy) was calculated for the overall cohort. Bivariate analysis (chi-square) was used to determine the unadjusted association of patient, tumor, and operative characteristics with receipt of preoperative biliary stenting. Chi-square tests were also used to compare the rates of each individual symptom between stented and unstented patients as well as between patients stented before and after seeing a surgeon. Multivariate logistic regression analysis was used to determine factors independently associated with preoperative biliary stenting.

Significance was accepted at the $P < .05$ level. Statistical analysis was carried out using SAS v 9.2 (Cary, N.C.).

RESULTS

Patient demographics and tumor characteristics. We found 2,573 patients who had undergone curative-intent surgical resection for adenocarcinoma of the head of the pancreas. The mean age at presentation was 73.8 ± 5.4 years. The majority of patients were female, white, and married; 2,318 patients (90.1%) had locoregional disease. Of the patients, 147 (5.7%) received neoadjuvant therapy in the 6 months prior to surgical resection. The distribution by SEER region is shown in Table II. Potential indications for preoperative biliary drainage, including jaundice, cholangitis, pruritus, and coagulopathy, were seen preoperatively in 64.1%, 10.3%, 6.5%, and 0.7% of patients, respectively. Tumor characteristics are shown in Table II.

Preoperative biliary drainage. Preoperative biliary drainage was performed in 1,354 patients (52.6%). Of these, 81.1% of patients underwent ERCP with endostenting, and 24.7% underwent percutaneous biliary drainage. Of the patients who underwent preoperative biliary drainage, 75.3 % underwent endostenting only, 18.9% underwent

Table II. Patient demographics and tumor characteristics

	Number (%) N = *2,573*
Patient demographics	
Age (mean ± SD, years)	73.8 ± 5.3
Female	1,400 (54.4)
Race	
White	2,222 (86.4)
Black	164 (6.4)
Hispanic	30 (1.2)
Other	157 (6.1)
Married	1,578 (62.9)
Charlson comorbidity score	
0	1,136 (44.1)
1	826 (32.1)
2	360 (14.0)
3+	251 (9.8)
SEER region	
Atlanta	88 (3.4)
Connecticut	257 (10.0)
Detroit	304 (11.8)
Greater California	331 (12.9)
Hawaii	57 (2.2)
Iowa	181 (7.0)
Kentucky	150 (5.8)
Los Angeles	229 (8.9)
Louisiana	125 (4.9)
New Jersey	371 (14.4)
New Mexico	62 (2.4)
San Francisco	101 (3.9)
San Jose	95 (3.7)
Seattle	120 (4.7)
Utah	99 (3.9)
Preoperative signs/symptoms	
Jaundice	1,650 (64.3)
Cholangitis	265 (10.3)
Pruritis	168 (6.5)
Coagulopathy	17 (0.7)
Tumor characteristics and treatment	
Local/regional stage	2,318 (90.1)
Tumor size in cm (N = 2,269)	3.3 ± 1.7
Well/moderately differentiated	1,414 (55.0)
Positive lymph nodes (N = 2,304)	1,402 (60.9)
Neoadjuvant therapy	147 (5.7)

percutaneous stenting only, and 5.8% underwent both procedures. In the 5.8% of patients (N = 78) who received both endostenting and percutaneous drainage, 38.5% received the procedures on the same day (N = 30); 24.4% received the endostent first (N = 19); and 37.2% received the percutaneous biliary drain first (N = 29). In patients who received a percutaneous transhepatic cholangiographic stent only, 82% had an ERCP without endostent placement prior to receiving a percutaneous transhepatic cholangiographic stent.

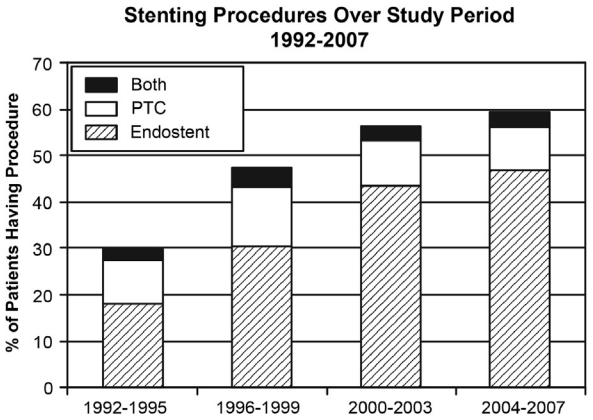

Fig 2. Trends in stenting over study period, 1992–2007. Preoperative biliary stenting increased steadily over the study period, from 29.6% of patients in 1992–1995 to 59.1% of patients in 2004–7, $P < .0001$. This increase is accounted for primarily by an increase in the rate of endostenting, from 20.2% of patients in 1992–1995 to 49.8% in 2004–2007 ($P < .0001$).

Time trends in preoperative biliary drainage. Preoperative biliary stenting increased from 29.6% of patients in 1992–1995 to 59.1% in 2004–2007 (Fig 2; $P < .0001$); this trend was attributed primarily to an increase in the use of endostenting. The rate of endostenting increased significantly over time, from 20.2% in 1992–1995 to 49.8% in 2004–2007 (Fig 2; $P < .0001$). The use of percutaneous stenting started at 11.5% in 1992–1995, peaked in the 1996–1999 period at 16.7%, then returned to approximately 12% for the later 2 time periods (Fig 2; $P = .16$). All time trends were identical when SEER regions that joined in 2001 were excluded (New Jersey, Kentucky, greater California, and Louisiana).

Concurrent increase in use of other tests. During the same period, the use of several other diagnostic tests increased as well. Between 1992 and 1995 and between 2004 and 2007, the use of MRI increased from 1.5% to 21.6% ($P < .0001$); CT use increased from 87.3% to 96.4%; and endoscopic ultrasound use increased from 2.7% in 1992–1995 to 16.8% in 2004–2007 ($P < .0001$). Trends for all tests are shown in Figure 3.

Of the 1,354 patients who underwent preoperative biliary stenting, 97.1% underwent CT, 20.5% underwent MRI, and 19.9% underwent EUS. Of these, 83.7% of CT scans, 53.1% of MRIs, and 12.2% of EUSs were performed prior to stenting, suggesting that staging before stenting occurred in most patients.

Timing of preoperative biliary stenting and surgeon/gastroenterologist visits. For the overall

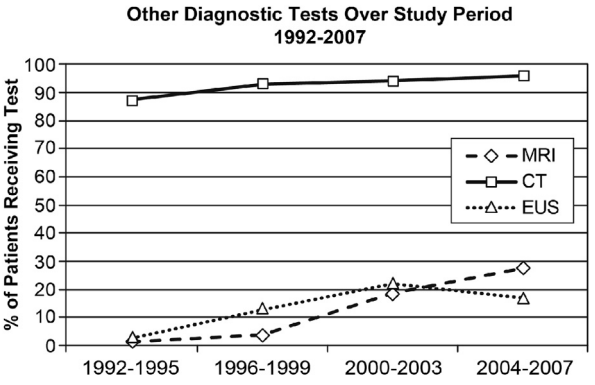

Fig 3. Trends in use of other diagnostic tests, 1992–2007. Preoperative diagnostic test use increased significantly during the study period. Computed tomography (CT) use increased from 87.3% to 96.4%, MRI from 1.5% to 21.6%, and EUS from 2.7% to 16.8% ($P < .0001$ for all).

cohort, we were unable to identify a surgeon visit in 443 patients (17.2%). In the 1,354 patients who underwent preoperative biliary stenting, we identified preoperative surgeon visits in 1,157 (85.4%). The date of surgery was the first surgeon-related claim in 14.6%. The preoperative biliary stent was placed prior to surgical evaluation in 77.7% of stented patients ($N = 1,052$). This decreased to 73.9% when we included only those with documented preoperative surgeon visits. Of the patients, 1,509 (58.7%) saw a gastroenterologist prior to seeing a surgeon. This pattern was consistent throughout the study period for all stented patients ($P = .55$); for those who saw a surgeon before surgery ($P = .25$); and when the SEER regions joining in 2000 were excluded ($N = 800$, $P = .31$).

Timing of preoperative biliary stenting and surgical resection. There was a longer time from diagnosis to surgery in stented than in unstented patients (mean, 41.0 ± 42.7 days vs 32.4 ± 45.8 days; median, 30 days vs 21 days, $P < .0001$). In patients who underwent preoperative biliary drainage, 69.6% had an interval of longer than 2 weeks between stent placement and surgery. The mean time from stenting to surgical resection was 35.0 ± 35.9 days (median, 23 days; interquartile range, 12–42 days). Additional stenting procedures and/or stent changes were required in 234 (17.3%) of stented patients prior to surgical intervention, and 4.7% ($N = 11$) of these patients had cholangitis prior to the initial stent placement. Overall, 174 patients (12.9%) had documented cholangitis after initial stent placement. Of those patients with cholangitis after stenting, none had had cholangitis documented prior to initial stent placement.

In the group of patients who underwent preoperative biliary stenting, those who were stented prior to seeing a surgeon had a longer time from stenting to surgical resection compared to those who were stented after seeing a surgeon (mean, 38.6 ± 37.3 days vs 25.3 ± 29.7 days; median, 26 days vs 14 days, $P < .0001$). When we included only those with a documented surgeon evaluation prior to resection, the time from surgical consultation to surgical resection remained longer for stented compared to unstented patients (mean, 24.2 ± 28.34 days vs 17.2 ± 26.21 days; median: 15 days vs 8 days, $P < .0001$).

Factors predicting biliary stenting. In an unadjusted analysis (Table III), stenting increased with year of diagnosis. Men were more likely to undergo preoperative biliary stenting than women ($P = .05$). Compared to black patients, white or Hispanic patients had higher rates of stenting ($P = .04$). Patients in the lowest income ($P = .0006$) and education quartiles ($P = .02$) were less likely to be stented. The use of stenting was similar across Charlson comorbidity scores. Preoperative biliary stenting rates varied across SEER regions, with rates above 60% in Kentucky, rural Georgia, Seattle, and Utah and less than 45% in Detroit, Hawaii, and Louisiana ($P < .0001$). There was no difference in patient demographics, preoperative symptoms, or tumor characteristics across SEER regions with enough patients to compare. Age was similar in the stented and unstented groups (73.6 ± 5.2 years vs 73.9 ± 5.4 years; $P = .19$).

Preoperative biliary stenting was more common in patients with preoperative jaundice, cholangitis, pruritus, or coagulopathy. Of jaundiced patients, 66.2% underwent stenting compared to 28.3% of patients without jaundice ($P < .0001$). Similarly, patients with preoperative cholangitis (87.5% vs 48.6%, $P < .0001$); pruritus (74.4% vs 51.1%, $P < .0001$); and coagulopathy (76.5% vs 52.5%, $P = .05$) were more likely to be stented than patients without the sign or symptom. However, stenting was also common in patients without these documented symptoms. We also evaluated time trends in symptoms coded in the Medicare claims to see whether there was a change in the presentations of patients or in the documentation of their presentations over time. There was no change in the number of patients with jaundice, ranging from 39% in 1992–1995 to 37% in 2004–2007 ($P = .48$). Only 168 patients had documented pruritus, and this increased slightly over time from 3% to 9% ($P = .005$). Likewise, only 265 patients had cholangitis, but the percentage of patients with

Table III. Bivariate analysis: factors associated with receipt of preoperative biliary stenting

	% *undergoing preoperative biliary stenting*	P *value*
Year of diagnosis		<.0001
1992–1995	29.6%	
1996–1999	47.1%	
2000–2003	55.9%	
2004–2007	59.1%	
Patient demographics		
Sex		.05
Male	54.7%	
Female	50.9%	
Race		.04
White	53.7%	
Black	45.7%	
Hispanic	56.7%	
Other	44.6%	
Marital status		.21
Married	53.6%	
Unmarried	51.1%	
Charlson comorbidity score		.36
0	52.2%	
1	51.0%	
2	55.6%	
3+	55.8%	
Income quartiles		.0006
Quartile 1 (lowest)	45.6%	
Quartile 2	55.6%	
Quartile 3	55.2%	
Quartile 4 (highest)	54.4%	
Education quartiles		.02
Quartile 1 (lowest)	47.5%	
Quartile 2	55.6%	
Quartile 3	54.6%	
Quartile 4 (highest)	53.2%	
SEER region		<.0001
Atlanta	53.4%	
Connecticut	51.0%	
Detroit	44.7%	
Greater California	56.5%	
Hawaii	40.4%	
Iowa	49.2%	
Kentucky	62.0%	
Los Angeles	47.2%	
Louisiana	43.2%	
New Jersey	59.3%	
New Mexico	45.2%	
Rural Georgia	66.7%	
San Francisco	46.5%	
San Jose	51.6%	
Seattle	63.3%	
Utah	64.6%	
Preoperative signs/symptoms		
Jaundice		<.0001
Yes	66.2%	
No	28.3%	
Cholangitis		<.0001
Yes	87.6%	
No	48.6%	
Pruritus		<.0001
Yes	74.4%	
No	51.1%	
Coagulopathy		.05
Yes	76.5%	
No	52.5%	
Tumor characteristics and treatment		
Stage (N = 2,496)		.0002
Localized	44.1%	
Regional	55.0%	
Distant	47.8%	
Differentiation		.49
Poor	53.7%	
Nodal status (regional disease only) (N = 1,979)		.22
Positive	55.7%	
Negative	52.7%	
Neoadjuvant therapy		.008
Yes	63.3%	
No	52.0%	
Gastroenterologist visit before surgeon visit		<.0001
Yes	60.7%	
No	41.2%	

cholangitis increased from 5% to 13% (P=.003). Coagulopathy was stable over time at about 1% (P=.47).

In patients undergoing preoperative biliary stenting, tumor size was larger than in patients who were not stented (3.5 ± 1.8 cm vs. 3.1 ± 1.6 cm, $P < .0001$). Stenting was more common in patients with regional disease.

Preoperative biliary stenting was more common in the 147 patients undergoing neoadjuvant therapy than in patients who were not (63.3% vs 52.0%, P = .008). Finally, patients who saw a gastroenterologist prior to seeing a surgeon were more likely to undergo preoperative biliary stenting (60.7% vs 41.2%, $P < .0001$).

There was no significant difference in the frequency of jaundice, cholangitis, or pruritus between the groups of patients stented before and after seeing a surgeon. Patients who were stented after seeing a surgeon were more likely to be coagulopathic than were patients who were stented before seeing a surgeon (P = .0006).

Table IV. Multivariate analysis: factors associated with preoperative biliary stenting

Factor	*Odds ratio*	*95% CI*
Patient demographics		
Age (per year)	0.99	0.97–1.01
Year of diagnosis	1.09	1.06–1.12
Male (female)	1.14	0.92–1.41
Race		
White	0.95	0.61–1.47
Hispanic	1.27	0.45–3.59
Black	Reference	Reference
Other	0.88	0.47–1.66
Married (unmarried)	1.13	0.91–1.41
Income quartiles		
Quartile 1	Reference	Reference
Quartile 2	1.29	0.93–1.80
Quartile 3	1.15	0.78–1.71
Quartile 4	1.05	0.67–1.67
Education		
Quartile 1	Reference	Reference
Quartile 2	1.24	0.89–1.72
Quartile 3	1.20	0.82–1.76
Quartile 4	1.01	0.66–1.57
SEER Region*		
Atlanta	1.72	0.83–3.55
Connecticut	2.02	1.10–3.71
Detroit	1.66	0.93–2.97
Greater California	1.90	1.09–3.31
Hawaii	1.11	0.44–2.80
Iowa	1.48	0.80–2.74
Kentucky	2.62	1.36–2.05
Louisiana	Reference	Reference
Los Angeles	2.02	1.10–3.71
New Jersey	1.79	1.01–3.15
New Mexico	0.84	0.33–2.12
San Francisco	1.53	0.75–3.12
San Jose	1.94	0.92–4.06
Seattle	3.89	1.98–7.65
Utah	3.37	1.66–6.88
Preoperative signs/symptoms		
Jaundice (no jaundice)	5.53	4.40–6.95
Cholangitis (no cholangitis)	6.33	3.98–10.08
Pruritus (no pruritus)	1.58	1.02–2.45
Coagulopathy (no coagulopathy)	2.119	0.53–8.44
Tumor characteristics and treatment		
Tumor size (per 10 mm)	0.99	0.98–0.99
Stage		
Localized	Reference	Reference
Regional	1.26	0.90–1.78
Distant	1.10	0.64–1.90
Differentiation (N = 2,229)		
Poor (vs none)	0.87	0.70–1.08
Nodal status (N = 2,304)		
Positive	1.10	0.87–1.40
Negative	Reference	Reference
Neoadjuvant therapy		
Yes (vs no)	2.71	1.58–4.66
Gastroenterologist visit before surgeon visit		
Yes (vs no)	1.80	1.46–2.22

*Louisiana was chosen as the reference because of low usage of preoperative biliary stenting amid a sizable patient population. Rural Georgia was excluded because of few patients (N = 3).

On multivariate logistic regression analysis (Table IV), the following factors were independently associated with receiving a preoperative biliary stent: later year of diagnosis, preoperative jaundice and cholangitis, larger tumor size, neoadjuvant therapy, and gastroenterologist visit prior to surgeon visit. The likelihood of undergoing preoperative biliary stenting varied significantly with SEER region. There was no difference in patient/tumor characteristics across SEER regions.

DISCUSSION

Despite evidence of increased complication rates and recommendations to avoid routine preoperative biliary stenting, the use of preoperative biliary stenting doubled between 1992 and 2007. The increase in preoperative biliary stenting was driven by a rise in the use of endostenting, whereas percutaneous stenting was used at a constant rate throughout the study period. Our population-based study found that 77% of patients are referred to a surgeon with a stent already in place, consistent with previous single-institution studies reporting rates of 42% to 79%.[26-29] Moreover, evaluation by a gastroenterologist prior to evaluation by a surgeon was associated with increased likelihood of stenting.

The literature surrounding the issue of preoperative biliary stenting has long generated controversy amidst evolving stent technology and techniques, and advances in surgical technique and perioperative care. Several large retrospective analyses comparing stented to unstented patients demonstrated either no difference in outcome[9-11] or increased rates of mortality,[14] overall complications,[13,14,27] overall infectious complications,[14,30] wound infection,[13-17,19,27,30] intraabdominal abscess,[13,14,30] or pancreatic fistula formation[15,27,30] with preoperative biliary stenting. Two meta-analyses in 2002[18,21] showed no difference in outcome between stented and unstented patients, and later meta-analyses in 2010 and

2011 demonstrated increased infectious complications.[19,20] A multicenter randomized controlled trial by van der Gaag et al in 2010 assigned patients to either an early surgery group (resection within 1 week of diagnosis) or a drainage group (endostenting with a 4- to 6-week drainage period prior to surgery).[22] The severe complication rates in the early surgery group and the biliary drainage group were 39% and 74%, respectively (relative risk = 0.54; 95% CI: 0.41–0.71; $P < .0001$). A significant proportion of complications were related to the stenting procedure itself and not to postoperative complications.

To our knowledge, our study is the first to evaluate trends in preoperative biliary stenting at the population level. In our multivariate analysis, we observed that patient symptoms and signs (jaundice, cholangitis, pruritus) were most strongly associated with biliary stenting, consistent with prior observations.[9,14,15,31] However, stenting was also performed in 28% of patients without documented jaundice and in approximately 50% of patients without cholangitis, pruritus, or coagulopathy. In addition, we observed significant geographic variation in the use of preoperative biliary stenting, with no evidence of differences in patient characteristics across SEER regions. This suggests that stenting was done based on provider preference and not on the characteristics of patients or tumors.

Preoperative biliary stenting is indicated in patients who will undergo neoadjuvant therapy prior to surgical intervention. Previous studies have documented the safety and efficacy of preoperative stenting in this setting.[32-34] In our study, only 147 patients underwent neoadjuvant therapy. Of these patients, 93 (63.3%) underwent preoperative stenting. In the setting of neoadjuvant therapy, stenting is appropriate to palliate jaundice while awaiting completion of therapy and restaging. However, of the 2,426 patients who did not undergo neoadjuvant therapy, 1,261 (52.0%) underwent preoperative biliary stenting. The observed increase in biliary stenting is not explained by an increase in receipt of neoadjuvant therapy in our cohort because the use of neoadjuvant therapy did not change over time.

The median time from stenting to surgical resection was 35 days, and 70% of patients had delays of greater than 2 weeks from stenting to resection. Consistent with the recent randomized controlled trial,[22] we also observed significant complication rates related to the stenting procedure. Our study demonstrated that 13% of stented patients developed documented cholangitis, and 17% required additional stenting procedures or stent changes prior to resection. A 2002 meta-analysis of randomized controlled trials reported drainage-procedure-related complications in 27.4% and stent dysfunction in 33.8% of patients.[18] Previous studies have documented hepatotoxicity, stent migration, and cholangitis as factors that may delay resection and may account for the long delay between stenting and surgical resection.[10,33,35,36] Conversely, the need for stent changes and development of cholangitis may be secondary to the delay and not vice versa.

The delay between diagnosis to resection was longer if the stent was placed prior to surgical evaluation, consistent with previous studies suggesting longer times to surgery for stented patients.[9-11,27] It is well documented that preoperative biliary stenting colonizes the biliary tree with enteric flora.[12,19,27,28,35,37,38] In addition, colonization and infection increase with increased duration of stenting and the presence of biliary contamination/infection is associated with increased rates of postoperative infectious complications and mortality.[10,19,27,28,35]

Our study has several limitations. First, laboratory results such as bilirubin levels and liver function tests are not available in the SEER-Medicare data. Second, symptoms such as jaundice, cholangitis, coagulopathy, and pruritis are likely to be undercoded in claims data. Thus, we may overestimate stenting in asymptomatic patients. For example, it is possible that patients in the non-jaundiced group (ie, no claim for jaundice) actually had mildly elevated bilirubin or alkaline phosphatase levels, meaning that the denominator would be lower.

In 14.6% of stented patients, we were unable to identify a surgeon visit prior to resection. We suspect that many of these patients were seen by surgeons as inpatients, and the surgeon's visit was not documented in the hospital claim. It is also possible that there are errors in the Medicare physician specialty codes. For this reason, we evaluated stenting prior to surgical evaluation both in the overall cohort (using the date of surgery as the date of surgeon visit when no preoperative visit was identified) and in the subgroup with identified preoperative surgeon consultations. Finally, as our study goes through 2007, several of the studies recommending against its use occurred after the time period of our study, and recent trends may have changed.

There are many situations, even in resected patients, in which stenting is warranted. For

example, stenting is appropriate in patients who need neoadjuvant chemoradiation and in patients with severe symptoms related to jaundice. Stenting may also be indicated in patients with significant comorbid medical illnesses who need further evaluation and optimization or stabilization of their medical conditions prior to surgery. In addition, stenting may be unavoidable in settings in which operating room, surgeon, or patient availability is limited. There was no concomitant increase in jaundice over time to suggest that the increase in stenting is clinically justified. Pruritus and cholangitis increased slightly over time. Although it is impossible to tell whether this increase represents a true change in symptoms or better coding, the small number of patients involved does not explain the doubling in stent rates. We cannot determine the appropriateness of stenting in any specific instance, but the increasing trend is of concern in light of consistent recommendations against the routine use of biliary stenting. Furthermore, geographic variation in the use of stenting, coupled with an increase in the use of many other preoperative tests (EUS, MRI, CT), suggests a more widespread problem of overuse.[39-43] In stented patients, the majority of diagnostic and staging tests were performed prior to stenting, suggesting careful staging. This provides additional evidence that referral patterns, and not the clinical picture, are driving preoperative biliary stenting; patients with staged, resectable disease are often being referred to gastroenterology before surgical evaluation without communication between the 2 specialties.

In conclusion, we demonstrated that preoperative biliary stenting has increased at an alarming rate despite consistent recommendations against its use. The majority of stenting occurred prior to surgical evaluation and was more likely if patients had symptoms or were seen by a gastroenterologist first. Biliary stenting was associated with a delay to surgery, which may have been due to stenting-related complications. These findings highlight the need for early communication between gastroenterologists and surgeons in the care of patients with pancreatic and other periampullary cancers. Multidisciplinary tumor boards are potential means to reduce unnecessary stenting and improve patient outcomes. Early surgeon involvement and multidisciplinary care offer opportunities for streamlining the evaluation of patients with early-stage pancreatic cancer to avoid unnecessary procedures and improve processes of care for this population of patients.

The collection of the California cancer incidence data used in this study was supported by the California Department of Public Health as part of the statewide cancer reporting program mandated by California Health and Safety Code Section 103885; the National Cancer Institute's Surveillance, Epidemiology and End Results Program under contract N01-PC-35136 awarded to the Northern California Cancer Center, contract N01-PC-35139 awarded to the University of Southern California, and contract N02-PC-15105 awarded to the Public Health Institute; and the Centers for Disease Control and Prevention's National Program of Cancer Registries, under agreement #U55/CCR921930-02 awarded to the Public Health Institute. The ideas and opinions expressed herein are those of the authors, and endorsement by the State of California, Department of Public Health, the National Cancer Institute, and the Centers for Disease Control and Prevention or their contractors and subcontractors is not intended nor should it be inferred. The authors acknowledge the efforts of the Applied Research Program, NCI; the Office of Research, Development and Information, CMS; Information Management Services (IMS), Inc; and the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in the creation of the SEER-Medicare database.

REFERENCES

1. Denning DA, Ellison EC, Carey LC. Preoperative percutaneous transhepatic biliary decompression lowers operative morbidity in patients with obstructive jaundice. Am J Surg 1981;141:61-5.
2. Gundry SR, Strodel WE, Knol JA, et al. Efficacy of preoperative biliary tract decompression in patients with obstructive jaundice. Arch Surg 1984;119:703-8.
3. Lygidakis NJ, van der Heyde MN, Lubbers MJ. Evaluation of preoperative biliary drainage in the surgical management of pancreatic head carcinoma. Acta Chir Scand 1987;153: 665-8.
4. Trede M, Schwall G. The complications of pancreatectomy. Ann Surg 1988;207:39-47.
5. Smith RC, Pooley M, George CR, et al. Preoperative percutaneous transhepatic internal drainage in obstructive jaundice: a randomized, controlled trial examining renal function. Surgery 1985;97:641-8.
6. Hatfield AR, Tobias R, Terblanche J, et al. Preoperative external biliary drainage in obstructive jaundice: a prospective controlled clinical trial. Lancet 1982;2:896-9.
7. McPherson GA, Benjamin IS, Hodgson HJ, et al. Pre-operative percutaneous transhepatic biliary drainage: the results of a controlled trial. Br J Surg 1984;71:371-5.
8. Pitt HA, Gomes AS, Lois JF, et al. Does preoperative percutaneous biliary drainage reduce operative risk or increase hospital cost? Ann Surg 1985;201:545-53.

9. Martignoni ME, Wagner M, Krähenbühl L, et al. Effect of preoperative biliary drainage on surgical outcome after pancreatoduodenectomy. Am J Surg 2001;181:52-9; discussion 87.
10. Jagannath P, Dhir V, Shrikhande S, et al. Effect of preoperative biliary stenting on immediate outcome after pancreaticoduodenectomy. Br J Surg 2005;92:356-61.
11. Sewnath ME, Birjmohun RS, Rauws EA, et al. The effect of preoperative biliary drainage on postoperative complications after pancreaticoduodenectomy. J Am Coll Surg 2001;192:726-34.
12. Karsten TM, Allema JH, Reinders M, et al. Preoperative biliary drainage, colonisation of bile and postoperative complications in patients with tumours of the pancreatic head: a retrospective analysis of 241 consecutive patients. Eur J Surg 1996;162:881-8.
13. Heslin MJ, Brooks AD, Hochwald SN, et al. A preoperative biliary stent is associated with increased complications after pancreatoduodenectomy. Arch Surg 1998;133:149-54.
14. Povoski SP, Karpeh MS, Conlon KC, et al. Association of preoperative biliary drainage with postoperative outcome following pancreaticoduodenectomy. Ann Surg 1999;230: 131-42.
15. Sohn TA, Yeo CJ, Cameron JL, et al. Do preoperative biliary stents increase postpancreaticoduodenectomy complications? J Gastrointest Surg 2000;4:258-67; discussion 267-8.
16. Pisters PW, Hudec WA, Hess KR, et al. Effect of preoperative biliary decompression on pancreaticoduodenectomy-associated morbidity in 300 consecutive patients. Ann Surg 2001;234:47-55.
17. Hodul P, Creech S, Pickleman J, et al. The effect of preoperative biliary stenting on postoperative complications after. Am J Surg 2003;186:420-5.
18. Sewnath ME, Karsten TM, Prins MH, et al. A meta-analysis on the efficacy of preoperative biliary drainage for tumors causing obstructive jaundice. Ann Surg 2002;236:17-27.
19. Garcea G, Chee W, Ong SL, et al. Preoperative biliary drainage for distal obstruction: the case against revisited. Pancreas 2010;39:119-26.
20. Qiu YD, Bai JL, Xu FG, et al. Effect of preoperative biliary drainage on malignant obstructive jaundice: a meta-analysis. World J Gastroenterol 2011;17:391-6.
21. Saleh MM, Nørregaard P, Jørgensen HL, et al. Preoperative endoscopic stent placement before pancreaticoduodenectomy: a meta-analysis of the effect on morbidity and mortality. Gastrointest Endosc 2002;56:529-34.
22. van der Gaag NA, Rauws EA, van Eijck CH, et al. Preoperative biliary drainage for cancer of the head of the pancreas. N Engl J Med 2010;362:129-37.
23. SEER-Medicare: Brief Description of the SEER-Medicare Database, November 2009. Available at http://healthservices.cancer.gov/seermedicare/overview/.
24. Research, Statistics, Data & Systems. Available at http://www.cms.gov/Research-Statistics-Data-and-Systems/Research-Statistics-Data-and-Systems.html.
25. Young JL RS, Ries LAG, Fritz AG, Hurlbut AA (eds.) SEER Summary Staging Manual, 2000: Codes and Coding Instructions. National Cancer Institute, NIH Pub. No. 01–4969, Bethesda, MD: NCI; 2001.
26. Isla AM, Griniatsos J, Riaz A, et al. Pancreaticoduodenectomy for periampullary malignancies: the effect of bile colonization on the postoperative outcome. Langenbecks Arch Surg 2007;392:67-73.
27. Morris-Stiff G, Tamijmarane A, Tan YM, et al. Pre-operative stenting is associated with a higher prevalence of post-operative complications following pancreatoduodenectomy. Int J Surg 2011;9:145-9.
28. Cortes A, Sauvanet A, Bert F, et al. Effect of bile contamination on immediate outcomes after pancreaticoduodenectomy for tumor. J Am Coll Surg 2006;202:93-9.
29. Coates JM, Beal SH, Russo JE, et al. Negligible effect of selective preoperative biliary drainage on perioperative resuscitation, morbidity, and mortality in patients undergoing pancreaticoduodenectomy. Arch Surg 2009;144:841-7.
30. Srivastava S, Sikora SS, Kumar A, et al. Outcome following pancreaticoduodenectomy in patients undergoing preoperative biliary drainage. Dig Surg 2001;18:381-7.
31. Herzog T, Belyaev O, Hessam S, et al. Bacteribilia with resistant microorganisms after preoperative biliary drainage: the influence of bacteria on postoperative outcome. Scand J Gastroenterol 2012;47:827-35.
32. Gerke H, White R, Byrne MF, et al. Complications of pancreaticoduodenectomy after neoadjuvant chemoradiation in patients with and without preoperative biliary drainage. Dig Liver Dis 2004;36:412-8.
33. Pisters PW, Hudec WA, Lee JE, et al. Preoperative chemoradiation for patients with pancreatic cancer: toxicity of endobiliary stents. J Clin Oncol 2000;18:860-7.
34. Eshuis WJ, van der Gaag NA, Rauws EA, et al. Therapeutic delay and survival after surgery for cancer of the pancreatic head with or without preoperative biliary drainage. Ann Surg 2010;252:840-9.
35. Povoski SP, Karpeh MS, Conlon KC, et al. Preoperative biliary drainage: impact on intraoperative bile cultures and infectious morbidity and mortality after pancreaticoduodenectomy. J Gastrointest Surg 1999;3:496-505.
36. Lai EC, Mok FP, Fan ST, et al. Preoperative endoscopic drainage for malignant obstructive jaundice. Br J Surg 1994;81:1195-8.
37. Herzog T, Belyaev O, Muller CA, et al. Bacteribilia after preoperative bile duct stenting: a prospective study. J Clin Gastroenterol 2009;43:457-62.
38. Groen AK, Out T, Huibregtse K, et al. Characterization of the content of occluded biliary endoprostheses. Endoscopy 1987;19:57-9.
39. Benarroch-Gampel J, Sheffield KM, Duncan CB, et al. Preoperative laboratory testing in patients undergoing elective, low-risk ambulatory surgery. Ann Surg 2012;256: 518-28.
40. Chung F, Yuan H, Yin L, et al. Elimination of preoperative testing in ambulatory surgery. Anesth Analg 2009; 108:467-75.
41. Schein OD, Katz J, Bass EB, et al. The value of routine preoperative medical testing before cataract surgery: study of medical testing for cataract surgery. N Engl J Med 2000;342:168-75.
42. Vogt AW, Henson LC. Unindicated preoperative testing: ASA physical status and financial implications. J Clin Anesth 1997;9:437-41.
43. Bryson GL, Wyand A, Bragg PR. Preoperative testing is inconsistent with published guidelines and rarely changes management. Can J Anaesth 2006;53:236-41.