Impact of drug-eluting stents on the comparative effectiveness of coronary artery bypass surgery and percutaneous coronary intervention

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Background Drug-eluting stents (DES) have largely replaced bare-metal stents (BMS) for percutaneous coronary intervention (PCI). It is uncertain, however, whether introduction of DES had a significant impact on the comparative effectiveness of PCI versus coronary artery bypass graft surgery (CABG) for death and myocardial infarction (MI).

Methods We identified Medicare beneficiaries aged ≥66 years who underwent multivessel CABG or multivessel PCI and matched PCI and CABG patients on propensity score. We defined the BMS era as January 1999 to April 2003 and the DES era as May 2003 to December 2006. We compared 5-year outcomes of CABG and PCI using Cox proportional hazards models, adjusting for baseline characteristics and year of procedure and tested for a statistically significant interaction (P_{int}) of DES era with treatment (CABG or PCI).

Results Five-year survival improved from the BMS era to the DES era by 1.2% for PCI and by 1.1% for CABG, and the CABG:PCI hazard ratio was unchanged (0.90 vs 0.90; P_{int} = .96). Five-year MI-free survival improved by 1.4% for PCI and 1.1% for CABG, with no change in the CABG:PCI hazard ratio (0.81 vs 0.82; P_{int} = .63). By contrast, survival-free of MI or repeat coronary revascularization improved from the BMS era to the DES era by 5.7% for PCI and 0.9% for CABG, and the CABG:PCI hazard ratio changed significantly (0.50 vs 0.57, P_{int} ≤ .0001).

Conclusions The introduction of DES did not alter the comparative effectiveness of CABG and PCI with respect to hard cardiac outcomes. (Am Heart J 2015;169:149-54.)

Percutaneous coronary intervention (PCI) has evolved considerably since its original introduction by Gruentzig in 1977,[1] with numerous technological improvements in the procedure as well as improvements in concomitant drug therapy and general management of patients with coronary disease. Two technologic innovations in PCI stand out against this background of continual incremental improvements: the approval of coronary stents in 1994 and the introduction of drug-eluting stents (DES) in 2004.[2] Coronary stents dramatically reduced the risk of acute vessel closure and of restenosis. Head-to-head trials comparing PCI using DES with PCI using bare metal stents (BMS) have shown that DES significantly reduced the rate of repeat procedures[3-5] without changing the rate of hard cardiac end points (death or myocardial infarction [MI]). The beneficial effect of DES on repeat procedures has led to their essentially replacing BMS during PCI.[6]

Percutaneous coronary intervention is an alternative to coronary artery bypass graft surgery (CABG) for treatment of multivessel coronary disease, and these procedures have been compared in a number of randomized trials.[7-9] Several waves of randomized trials have been conducted based on the widespread belief that newer PCI devices (first BMS, then DES) altered the comparative balance between CABG and PCI for patients with multivessel disease. The relative effectiveness of CABG and PCI upon mortality did not, however, differ significantly between randomized clinical trials in which PCI was performed using balloon angioplasty and trials in which PCI was performed using BMS,[9] and mortality has been lower after CABG compared with PCI in more recent trials that used DES for PCI.[10,11] The recently reported ASCERT study used observational data to compare CABG and PCI using DES and also found improved survival after CABG.[12]

The continuing evolution of medical technologies, such as PCI, presents a dilemma for evidence-based medical

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Supported by grant HL099872 from the National Heart Lung and Blood Institute, Bethesda, MD, with additional support from grant 0875162N from the American Heart Association, Dallas, TX. The sponsors had no role in study design, analysis, or reporting.
Submitted October 14, 2014; accepted October 14, 2014.
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http://dx.doi.org/10.1016/j.ahj.2014.10.004

Table. Baseline characteristics by treatment era and by treatment

	Era of treatment		Treatment received	
	BMS	DES	CABG	PCI
	(n = 38,277)	(n = 43,645)	(n = 40,961)	(n = 40,961)
Age				
66-70 y	29.3	30.5	30.0	29.9
71-75 y	28.2	27.3	27.6	27.8
76-80 y	23.4	23.0	23.1	23.3
81-85 y	14.2	14.7	14.5	14.5
≥86 y	4.8	5.6	4.8	4.6
Female	43.1	41.0	41.7	42.4
Race				
White	92.7	91.8	92.3	92.1
Black	4.3	4.9	4.6	4.7
Other	3.0	3.4	3.2	3.2
Diabetes	31.6	34.7	33.2	33.2
Hypertension	75.8	81.6	79.0	78.8
Hyperlipidemia	28.7	29.6	28.9	29.5
Tobacco abuse	17.3	20.9	18.9	19.5
Chronic kidney disease	4.2	5.8	5.0	5.1
Peripheral arterial disease	16.6	18.6	17.3	18.0
Cerebrovascular disease	15.8	17.3	16.5	16.8
Prior MI	13.7	9.1	11.0	11.5
Heart failure	14.2	12.1	12.7	13.4
Unstable angina	33.7	26.6	30.2	29.6
Atrial fibrillation/flutter	11.6	11.4	11.3	11.6
Stent used in PCI	92.9	97.2	–	95.2
IMA used in CABG	80.3	87.2	84.0	–

Abbreviation: *IMA*, internal mammary artery.

practice: have recent changes altered clinical outcomes to the extent that older evidence is out of date? This "moving target problem"[13,14] is especially acute in comparing CABG and PCI because each procedure continues to be refined, and background management of coronary disease continues to improve, which could lead to better outcomes after both procedures.[15-17] The need to compare clinical outcomes over long-term follow-up further complicates this assessment because 5-year results can only be assessed based on patients with ≥5 years of follow-up, who necessarily have been treated with earlier technology.

One potential solution to the moving target problem is to track outcomes over time using continuously collected data and then test explicitly for changes in comparative effectiveness. In this study, we therefore sought to test whether the comparative effectiveness of CABG and PCI on hard clinical outcomes has changed over time and specifically by the introduction of DES. We reasoned that a time series approach would allow us to isolate any specific effect of DES from general secular trends toward improved outcomes by comparing the difference in outcomes between CABG and PCI after the introduction of DES with this difference before the introduction of DES. We hypothesized that a "difference-in-differences" approach would directly test whether the availability of DES altered the balance between CABG and PCI on hard cardiac outcomes.

Methods

The study population consisted of fee-for-service Medicare beneficiaries who underwent either multivessel CABG or multivessel PCI between January 1999 and December 2006. To permit a 1-year look-back period to define comorbidities, we restricted the population to individuals aged ≥66 years who had both Part A and Part B coverage and were not in a Medicare health maintenance organization. We identified CABG and PCI procedures in the 20% sample of Medicare Part A data and defined relevant comorbidities using both Part A and Part B data.

We identified patients by *International Classification of Diseases, Ninth Revision* (*ICD-9*) procedure codes for multivessel CABG (36.12, 36.13, 36.14, 36.16, or 36.11 plus 36.15) or multivessel PCI (*ICD-9* code 36.05 and from October 2005 *ICD-9* code 00.66 and either an *ICD-9* code of 00.41, 00.42, 00.43, or a *Current Procedural Terminology* code of 92981 or 92984). We excluded patients who had single-vessel PCI or CABG, had concomitant cardiac procedures (such as valve replacement) at the time of CABG, were of unknown race, or