Review Article

Percutaneous Coronary Intervention in Stable Coronary Heart Disease—Is Less More?

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Summary

Background: This review concerns the putative benefit of percutaneous coronary intervention (PCI) over optimal medical therapy (OMT) for symptomatic patients with stable angina pectoris, or for asymptomatic persons in whom screening tests have revealed coronary heart disease (CHD; this entity has been newly designated chronic coronary syndrome, or CCS). Moreover, it addresses the question whether the indications for which PCI is now performed in Germany on patients with CCS are consistent with current scientific knowledge.

Methods: The pathophysiological concept of CHD and ischemia induction is discussed in the light of the scientific literature. This concept implies that PCI might be beneficial in the treatment of CCS. The benefit of PCI over OMT has now been evaluated in seven randomized trials (the so-called milestone trials). The current situation in Germany is presented here as well, on the basis of the available data.

Results: The pathophysiological concept of CHD implies that the particular coronary artery stenoses that are likely to give rise to a myocardial infarction (the so-called vulnerable plaques) cannot be identified prospectively with current methods. Moreover, a coronary artery stenosis will not necessarily cause myocardial ischemia. All of the randomized trials carried out to date that have compared OMT to PCI-plus-OMT in patients with CCS have led to the conclusion that PCI, because it focuses on individual coronary artery stenoses, cannot prolong survival or lower the incidence of myocardial infarction over the long term. This remains the case even if a single coronary artery stenosis is known to be causing moderate or severe myocardial ischemia (a conclusion of the ISCHEMIA trial). A PCI performed only because the coronary stenosis or stenoses meet certain morphological criteria, without any demonstration of a resulting functional disturbance, is generally detrimental to the health of the patient, with rare exceptions, and is inconsistent with the recommendations of current guidelines. The number of PCIs being performed in Germany at present is high compared to other countries; this arouses concern that the indications for it may be dubious in many cases.

Conclusion: Current data imply that PCI for CCS does not improve outcomes in a large percentage of cases. A symptomatic benefit exists only in patients with frequent angina pectoris. The selection of CCS patients for PCI needs to be more strictly bound to the recommendations of current guidelines, particularly in Germany.

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Percutaneous coronary intervention (PCI) improves symptoms and clinical outcome in patients who have acute coronary syndrome (ACS), i.e., who are hospitalized and undergo coronary angiography because of a coronary artery stenosis or occlusion with dynamic elevation of cardiac troponins in the blood (1). Many patients and physicians assume the same holds for chronic coronary syndrome (CCS). They suppose that eliminating a coronary artery stenosis lowers the risk of myocardial infarction or sudden cardiac death, even in patients with

stable angina pectoris and/or myocardial ischemia without dynamic troponin elevation.

Method

In this article, we discuss whether the above assumption, which is widely considered plausible, is consistent with known pathophysiology, and whether randomized, controlled trials have shown any beneficial effect on symptoms or clinical outcome from the elimination of coronary artery stenosis in patients with CCS.

We assessed randomized trials that met the following criteria:

- The effects of optimal medical therapy (OMT) and of PCI plus OMT were compared in patients with CCS.
- The PCI methods used were stated.
- Patients with ACS were excluded.
- Hemodynamic testing was performed, at least in some patients (only illustrations were available from the ISCHEMIA trial as of November 2019, and 26% of the patients in this trial underwent surgical revascularization).

We also assessed the randomized trials that compared two different criteria for establishing the indication for PCI, namely, a hemodynamic (functional) demonstration of coronary artery stenosis versus a solely morphological demonstration by coronary angiography. The results of these seven so-called milestone studies are summarized in *Table 1*.

To evaluate the frequency of PCI and the quality of the indications for it in Germany, we used statistics that were gathered for the purpose of international comparisons by the Organization for Economic Cooperation and Development (OECD) and by the German Heart Foundation, reviewing them in the light of recommendations contained in the guidelines of the European Society of Cardiology (2).

Results

Does every high-grade coronary artery stenosis impair blood flow in the coronary vessel and cause ischemia?

It is essential to maintain the distinction between the demonstration or exclusion of an epicardial coronary artery stenosis on the one hand, and the demonstration or exclusion of myocardial ischemia on the other.

The demonstration or exclusion of epicardial coronary artery stenoses

By definition, the classic demonstration or exclusion of an epicardial coronary artery stenosis is effectuated with invasive coronary angiography (cardiac catheterization). Cardiac computed tomography (CT) is a non-invasive investigation whose development has recently advanced to the point that it can sometimes be used for the same purpose (mainly to rule out a stenosis). Thus, a normal coronary CT often obviates the need for cardiac catheterization (3). These two techniques enable only the morphological assessment of a coronary artery stenosis, which cannot be assumed equivalent to the functional demonstration of stress-related ischemia or of the risk of a myocardial infarction.

Non-invasive methods of demonstrating or excluding myocardial ischemia

The non-invasive assessment of stress-induced myocardial ischemia is best performed with imaging techniques such as stress echocardiography, myocardial scintigraphy (SPECT = single photon emission

computed tomography), positron-emission tomography (PET), or stress magnetic resonance imaging (MRI). Stress MRI is a non-invasive diagnostic technique that in fact provides more precise guidance concerning the need for PCI than does coronary angiography with invasive pressure-wire measurement. In one study, the use of stress MRI lowered the rate of an indication for PCI from 45.0% to 35.7% ($p = 0.005$), without any unfavorable effect on symptoms or clinical outcome at 1 year (4). MRI for this purpose, however, is not currently reimbursed by the statutory health insurance carriers in Germany. As a rule, patients with suspected CCS should have a non-invasive test before cardiac catheterization if the pretest probability of significant coronary artery stenosis lies in the range of 15% to 85% (2).

According to the guidelines of the European Society of Cardiology, imaging studies should be performed in preference to stress electrocardiography (stress ECG), because they are more informative (2). The reported sensitivity of imaging studies for the demonstration of relevant epicardial coronary artery stenosis is 73–93%, while their specificity for the exclusion of a relevant stenosis is 53–87%. Stress MRI has the greatest precision of all imaging modalities (5). The standard for comparison is either morphological stenosis, demonstrated by coronary angiography, or else a pathological intracoronary functional test (fractional flow reserve [FFR], or, more recently, the instantaneous wave-free ratio [iFR] or resting full cycle ratio [RFR]). True stress ischemia can, however, be present because of microvascular hypoperfusion even when invasive diagnostic studies have ruled out a significant stenosis. In the ISCHEMIA trial, 20% of the patients suspected of having coronary heart disease (CHD) were found to have major ischemia in non-invasive imaging studies despite the absence of a demonstrable epicardial stenosis (6).

Anatomic reference methods such as invasive coronary angiography or coronary CT do not involve any assessment of the microcirculation. Microvascular anatomical changes or functional disturbances are associated with risk factors for atherosclerosis such as arterial hypertension, hyperlipidemia, and diabetes mellitus. They often lead to stress ischemia of the myocardium, even in the absence of an epicardial coronary artery stenosis. These microcirculatory disturbances are often interpreted as false positive findings of non-invasive imaging. This interpretation may be wrong, however, as an impairment of myocardial perfusion may indeed be present. On the other hand, in cases where more than 50% coronary artery stenosis has been demonstrated without any impairment of blood flow, a normal stress test, if found, is sometimes considered a false negative; yet no significant impairment of blood flow under stressful conditions is found in 37% of patients with $\geq 50\%$ coronary stenosis (7).

TABLE

Randomized milestone trials comparing PCI-plus-OMT vs. OMT in patients with stable CHD (= CCS)

Trial name →	COURAGE Trial (short) (24)	COURAGE Trial (long) (25)	Bart 2b Trial (31)	FAME I Trial (29)	FAME II Trial (34)	Orbita Trial (32)	ISCHEMIA Trial (6, 26, 27, 28, 33)
Total number of randomized patients	2287	1211	2368, of whom PCI vs. OMT was compared in 1605, ACVB vs. OMT in the rest	1005	888	196	5179
Median follow-up duration	4.6 years	11.9 years	5.3 years	1.0 year	5 years	6 weeks	5 years
Inclusion criteria	stenosis ≥ 70% + ischemia, or >80% + AP	see left	type 2 diabetes + CHD, stenosis ≥ 70%, or demonstration of ischemia	>2-vessel CHD, >50% stenosis, or PCI indicated	PCI > 50% stenosis with stable AP or silent ischemia	FFR ≤ 0.80 OMT; PCI (double-blind) in single-vessel disease	moderate to severe ischemia on stress test for CCS, exclusion criteria: HS > 50%, LVEF < 35%.
Objectives of trial	comparison of PCI vs. OMT for stable AP	see left	comparison of OMT vs. PCI or ACVB	comparison of functional vs. anatomic indications for PCI	Comparison: FFR ≤ 0.80: PCI vs. OMT, FFR ≥ 0.80: OMT	symptoms better after PCI compared to sham PCI	Benefit of Coro after prior CCT? In case of CCT: benefit of revascularization vs. OMT
Trial endpoints	mortality + MI	mortality	I. death + MI II. death + MI + stroke + UAP	I. combined: death + MI + need for revascularization, II. death or MI	I. death + MI + revascularization, II. death + MI	Differences in exercise tolerance?	CV death + MI + UAP + HF + resuscitation after cardiac arrest
Results	19.0% PCI vs. 18.5% OMT OR 1.05	25% PCI vs. 24% OMT OR 1.03	I. death 11.7% revascularization 12.1% OMT p = 0.87 II. 23.0% PCI, 21% OMT, p = 0.84; 22.2% CABG, 30.5% OMT, p = 0.07	I. 13.2% functional (FFR) 18.3% anatomic p = 0.02 II. MI + death 7.3% functional 11.1% anatomic p = 0.04	I. PCI 13.9%, OMT 27.0%, HR 0.46 (0.34–0.63); II. death or MI, HR 0.72 (0.50–1.03)	no significant difference in exercise tolerance on stress test (p = 0.1) or frequency of angina pectoris (p = 0.073), but PCI yielded a significantly higher rate of freedom from AP (49.5% vs. 31.5%) as well as improved stress echo findings	no significant difference between revascularization and OMT in the overall group or any subgroup, but improved quality of life in patients who had angina pectoris on inclusion
Randomization	PCI or OMT	see left	PCI or CABG vs. OMT with insulin or oral antidiabetic agents	PCI FFR < 0.80 versus anatomical angiographic estimation of stenosis > 50%	FFR ≤ 0.80 randomized PCI vs. OMT, FFR > 0.80 OMT	PCI vs. sham PCI for patients with FFR ≤ 0.80	revascularization (24% CABG, 76% PCI) vs. OMT
Remarks	highly selected patient group, >90% BMS	see left	34.7% DES, 56% BMS; no difference between PCI and OMT with respect to the primary or secondary endpoint; strong trend favoring CABG over OMT with respect to the secondary endpoint	both endpoints were significantly more common when an anatomic, rather than functional, indication criterion for PCI was used	No difference between OMT and PCI with respect to MI and overall mortality at 5 years, even in patients with FFR ≤ 0.80. Revascularization was, however, much more common in the PCI group, with a crossover rate of 51%.	This was the first double-blinded trial of the effect of PCI on symptoms	Milestone trial with slow recruitment: endpoints new and broadened. Case numbers: 8000 at outset, now fewer. Financed independently of industry, results now only available as a presentation from November 2019.
Conclusions	PCI had no effect on overall mortality or MI rate in patients with stable AP	No difference in mortality between PCI and OMT, even at 12 years; overall mortality low, similar to age-matched US population	PCI had no effect on survival or cardiac events even in patients with type II diabetes mellitus; CABG showed a strong trend toward improvement	PCI without functional testing of the stenosis is associated with a higher rate of death and myocardial infarction	Even with a functionally based PCI indication, PCI was no better than OMT (despite DES) with respect to overall mortality or MI, but PCI was significantly better when the 51% crossover to revascularization was taken into account.	The double-blinded trial showed no symptomatic benefit from PCI compared to OMT; however, case numbers and power were low. The PCI group had less ischemia on stress echo.	

AP, angina pectoris; ACVB, aortocoronary venous bypass; BMS, bare metal stents; CABG, coronary artery bypass grafting; CCS, chronic coronary syndrome; CCT, cardiac computerized tomography; CHD, coronary heart disease; Coro, coronary angiography; CV, cardiovascular; DES, drug-eluting stent; FFR, functional flow reserve; HF, heart failure; HR, hazard ratio; MI, myocardial infarction; MS, mainstem; OMT, optimal medical therapy; OR, odds ratio; PCI, percutaneous coronary intervention; UAP, unstable angina pectoris.

FIGURE 1

a Stenoses in the coronary system

b Infarction-inducing stenoses

Frequency distribution of stenoses in the coronary arterial system (a, b) and morphology of coronary vessel cross-sections (c–e):

- a) The bar graph depicts the frequency distribution of stenoses on coronary angiography, classified by degree of stenosis. Stenoses of less than 50% are the most common, accounting for ca. 80% of all stenoses.
- b) The bar graph shows what degree of stenosis precedes an infarction in a vessel's territory. Stenoses of less than 50% are the most common type in the vascular tree, and the type that most commonly leads to stenosis (so-called vulnerable plaques).
- c–e) Macroscopic cross-sections through various coronary artery stenoses:
 c) stable plaque; d) vulnerable plaque with atheroma in the tunica media; e) broken vulnerable plaque with vascular occlusion by thrombus.

Invasive methods of demonstrating or excluding functionally significant coronary artery stenosis

The pressure-wire method, which is now the method most commonly used, measures the drop in blood pressure across a stenosis, compared to the pressure in the aorta, after maximal vasodilatation of the peripheral vascular bed (FFR). A 20% or greater drop in blood pressure distal to the stenosis ($\text{FFR} \leq 0.8$) is considered hemodynamically significant (8–10). Aside from FFR, there are other ways to carry out measurements with a pressure wire that do not require vasodilatation (e.g., iFR, RFR, distal-to-aortic pressure ratio [Pd/Pa]).

There are also software-based methods of calculating FFR from the findings of coronary angiography. These methods yield figures that are well correlated with invasively measured FFR (11), but they have not yet been definitively validated for clinical use. Non-invasive methods such as CT-FFR have been developed so that the drop in blood flow

velocity across a stenosis can be estimated with CT-based algorithms; these are not widely used at present (12) and have not yet been definitively validated, either.

Does a high-grade coronary artery stenosis imply a risk of myocardial infarction?

CHD is defined as the presence of plaques that narrow the vascular lumen to a greater or lesser extent, and it is associated with a worse prognosis. The presence of CHD is correlated with a visible increase in coronary artery calcification on CT and with an elevated rate of cardiac events compared to persons with normal coronary arteries (13, 14). Stenoses of less than 50% seen on CT are associated with a mortality that is twice as high as in persons without plaques, after 3.1 years of follow-up (15). The rate of cardiac events is also higher, however, in persons with coronary microcirculatory impairment due to diabetes mellitus, arterial hypertension, or end-stage renal failure, independently of the presence or absence of epicardial coronary artery stenosis (16).

In fact, low-grade stenoses (stenoses that do not limit blood flow) are much more common in the diseased coronary arterial bed than high-grade stenoses (stenoses that do limit blood flow): approximately 80% of stenoses are of less than 50% (Figure 1a) (17). Low-grade stenosis can also cause myocardial infarction through the rupture of so-called vulnerable plaques, with release of the subendothelial lipid core and consequent acute thrombotic coronary artery occlusion (18). Clinical studies have shown that most myocardial infarctions arise from low-grade stenoses (19). This was determined by a review of older coronary angiograms in patients who underwent repeat angiography in the setting of a new, acute infarction (Figure 1b and Figure 2).

Vulnerable plaques cannot be identified by cardiac catheterization studies. Plaques can now be morphologically characterized with invasive and non-invasive imaging techniques (intravascular ultrasonography [IVUS], optical coherence tomography [OCT], MRI, CT coronary angiography). The identification of vulnerable plaques is currently a subject of intensive research, and there is as yet no justification for the early interventional treatment of such plaques (Figure 1 c–d).

Does PCI lower the rate of infarction and/or mortality?

Four meta-analyses that included older studies, some of which were not randomized, as well as observational studies without hemodynamic testing yielded the conclusion that surgical revascularization lowers both mortality and the reinfarction rate, while PCI, in contrast, does not lower either of these (20–23).

The COURAGE trial of 2007 was the first large-scale, randomized clinical trial in patients with CCS that compared PCI plus OMT with OMT alone. No benefit was found for PCI plus OMT, even after a follow-up interval of up to 12 years. Moreover, the two treatment groups had the same overall mortality, which, in turn, was nearly the same as that of the age- and sex-matched normal population (Figure 3) (24, 25). 50% of the patients in the OMT group did, however, undergo revascularization within five years because of undesired symptoms or the development of an acute coronary syndrome. In a subgroup of patients with marked myocardial ischemia (affecting more than 8% of the myocardium), it was found that PCI might indeed have a beneficial effect on outcome (24). The prospectively randomized ISCHEMIA trial was performed to answer this important question definitively (6, 26, 27).

The ISCHEMIA trial was carried out in more than 5000 patients with epicardial stenosing CHD (main-stem stenosis excluded, CCS, left-ventricular ejection fraction $\geq 35\%$, no severe symptoms) and moderate or severe ischemia. Revascularization (74% PCI, 26% bypass surgery) did not significantly lower the frequency of the primary combined endpoint, which consisted of death, myocardial infarction, hospitalization for unstable angina, congestive heart failure, or successful resuscitation after cardiac arrest, compared to OMT after more than 4 years of follow-up (13.3%

Figure 2: Coronary angiogram of a 64-year-old man with recurrent infarction due to a previously low-grade stenosis of the circumflex branch

- a) RAO projection of the coronary angiogram in this patient, who underwent emergency recanalization of the LAD (marked with a circle) after an acute anterior wall infarction due to LAD occlusion. The circumflex branch has an approximately 30% proximal stenosis (marked with a square).
- b) 12 weeks later, despite OMT, the patient presented once again with an acute coronary syndrome. The circumflex branch was found to be occluded (marked with a rectangle), even though the stenosis had been seen previously to be non-critical. The previously recanalized LAD displays mild narrowing of the lumen in the region of the stent (marked with a circle), but it is open.

This case illustration shows that stenoses of less than 50% can lead to vascular occlusion, in turn implying that the treatment of stenoses in stable CHD cannot lower the rate of infarction, because diffuse low-grade changes in the coronary vascular tree are not considered an indication for PCI.

CHD, coronary heart disease (= CCS); CX, circumflex branch; LAD, left anterior descending coronary artery; OMT, optimal medical treatment; PCI, percutaneous coronary intervention; RAO, right anterior oblique.

versus 15.5%, $p = 0.34$) (28). However, 23% of the patients in the conservative treatment group of this trial crossed over to invasive treatment over the course of follow-up.

The FAME-2 trial was a further attempt to demonstrate the putative benefit of PCI on clinical outcome in patients with demonstrated ischemia (29). Functionally relevant stenoses were measured with invasive FFR, and it was studied whether their elimination with PCI could lower the frequency of a combined primary endpoint that consisted of death, myocardial infarction, or emergency revascularization. Patients with appropriate FFR findings were randomly assigned to receive either OMT alone or OMT plus PCI. The latter group underwent fewer emergency (i.e., unplanned) coronary revascularization procedures than the former (6.3% vs. 21.1%). This was a main determinant of the significant reduction of the combined primary endpoint (death, myocardial infarction, urgent revascularization) in the OMT-plus-PCI group (13.9% versus 27%). 51% of the patients allotted to OMT group underwent a PCI within 5 years (just as in the COURAGE trial), but 13.4% of the patients in the OMT-plus-PCI group also underwent a (second) revascularization procedure in this period. The mortality at 5 years was the same in the two groups (5.1% versus 5.2%). There were more

FIGURE 3

Probability of long-term survival of American patients treated in the period 1999–2012

for chronic coronary syndrome, as a function of treatment modality and compared to the normal age- and sex-matched U.S. population.

In the COURAGE trial, patients were randomized to receive either a percutaneous coronary intervention (PCI) in combination with optimal medical treatment (OMT) or OMT alone, and the outcomes in the two groups were compared. As shown in the figure, no significant difference in mortality was observed at any time. It was also found that, whichever of the two treatment regimens was given, the mortality of the patients began to be mildly higher than that of the normal population only 6 years after the start of treatment (from: Sedlis SP, Hartigan PM, Teo KK, et al.: Effect of PCI on long-term survival in patients with stable ischemic heart disease. *N Engl J Med* 2015; 373: 1937–46 [25];reprinted with the kind permission of The New England Journal of Medicine).

FIGURE 4

The Heart Report of the German Heart Foundation states that about 900 000 left-heart catheterizations were performed in Germany in 2016. Some 600 000 of these were in patients with stable coronary heart disease, and, in turn, some 180 000 of the catheterizations in patients with stable disease were combined with a percutaneous coronary intervention (PCI).

myocardial infarctions in the OMT group (12.0% versus 8.1%); this finding barely failed to reach statistical significance (hazard ratio [HR] 0.66, 95% confidence interval [0.43; 1.00]) (30). Thus, the FAME-2 trial showed, in accordance with the previous findings of the ISCHEMIA trial, that the elimination of a hemodynamically significant epicardial stenosis does not further lower the already low mortality in this pa-

tient group. Moreover, the BARI-2b trial showed that PCI did not improve clinical outcome in patients with diabetes mellitus, either, despite their higher risk of myocardial infarction (31).

In a recent article on coronary artery bypass grafting (CABG), it was proposed that the lower long-term rates of myocardial infarction and death after CABG compared to PCI may be due to the ability of CABG to bypass lower-grade, but potentially vulnerable, stenoses by surgically induced collateralization (32).

Can PCI worsen outcomes in patients with functionally irrelevant stenoses?

The results of the FAME-1 trial suggest that this is, in fact, the case. Patients with anatomically high-grade stenoses revealed by angiography were randomly allotted to two groups: the patients in one group were treated with PCI on the basis of a morphological assessment alone, while the patients in the other group were treated with PCI only if the associated measured FFR value was less than or equal to 0.80. There were significantly more events in the first group (death or myocardial infarction: 11.1% versus 7.3%, $p = 0.04$). PCI was 37% more common in the former group, for which the indication for PCI was determined on morphological criteria alone (7). In general, it is clear that unnecessary PCIs can cause intra- and/or post-interventional myocardial infarction through coronary artery dissection or stent thrombosis.

Does PCI have a symptomatic benefit?

It has been shown in numerous registry studies and non-randomized studies that patients' symptoms improve after a PCI or bypass operation. It was not investigated, however, whether this effect might be achievable with OMT alone. In the ISCHEMIA trial mentioned above, patients with frequent angina pectoris and marked myocardial ischemia who were randomized to OMT plus revascularization (26% CABG, 74% PCI) had a statistically significant, lasting improvement of their quality of life compared to their counterparts who were randomized to OMT alone, and they were free of angina at 3 years (33).

In the FAME-2 and ORBITA trials, patients with hemodynamically significant stenoses were randomized to either PCI plus OMT or OMT alone, and their symptoms were studied. At 3 years, the PCI patients in the FAME-2 trial had significantly less frequent angina pectoris (5.2% versus 9.6%); a significant diminution of angina pectoris was no longer seen at five years, but 51% of the patients in the OMT group had undergone revascularization in the meantime (22). The FAME-2 trial was not blinded, however; the physician and the patient both knew which treatment had been performed, and a placebo effect of invasive treatment could not be ruled out. The ORBITA trial, which was the first double-blinded trial, included only 200 patients (34). During coronary angiography (FFR in both groups ≤ 0.80), the patients received either real or sham PCI. Exercise tolerance was slightly higher at six weeks in the PCI group, but the two groups did not differ significantly in the frequency of angina pectoris. This trial, although small in scale, was the first to

FIGURE 5

The number of coronary angioplasties and coronary artery bypass graft operations per 100 000 population in countries across Europe, 2014.

Germany had the highest number of percutaneous coronary interventions (PCI) per capita, approximately 70% more than Switzerland, a neighboring, mostly German-speaking country. (Source: OECD Health Statistics 2016; Eurostat Database); EU24, mean of 24 countries in the European Union.

demonstrate that invasive treatment has a clinically relevant placebo effect that should not be allowed to distort the assessment by patients and their physicians of the symptomatic benefit of PCI.

The situation in Germany

According to the German Heart Report, the number of cardiac catheterizations per year in Germany fell from 906 843 in 2014 to 880 886 in 2017, a 2.9% decline. Over the same period, however, the number of PCIs rose by 4.6%, to 378 152 in 2017 (35, 36). This was paralleled by a 9.4% increase in the number of cardiac catheterization laboratories in Germany, from 919 to 1005.

In 2014, more PCIs were performed per capita in Germany than in any other country in Europe, according to figures of the OECD (457 PCIs in Germany versus 258 PCIs in Europe per 100 000 persons per year, i.e., 78% more in Germany than the European average) (Figures 4 and 5). In the United States, the number of PCIs has fallen markedly (by 40% in some areas), as a consequence of the scientific evidence discussed here and improved transparency regarding indications. The German Institute for Quality Assurance and Transparency in Health Care (*Institut für Qualitätssicherung und Transparenz im Gesundheitswesen*, IQTIG) reports that, in cardiac catheterization laboratories in Germany, the mean value of the assessed quality indicator “noninvasively obtained evidence of ischemia as an indication for elective isolated coronary angiography” (QI-HD 56000) is only 55.6% (37). Moreover, according to the registry of the Working Group of Hospital Attending Cardiologists in Germany (*Arbeitsgemeinschaft Leitender Kardiologischer Krankenhausärzte e. V.*, ALKK) for the years

2010–2013, pressure-wire measurements were carried out in only 3.3% of the PCIs that were performed ad hoc over this period (38), even though PCI for stenoses that seem relevant by angiographic criteria alone is known to yield less favorable long-term results than PCI for stenoses with demonstrated functional impairment of coronary flow (7).

Opportunities for improvement

Why are far more cardiac catheterizations and PCIs performed per person in Germany than in other Western countries? Certain financial incentives in the German health-care system, which enable hospitals to subsist economically only if they have a cardiac catheterization laboratory, would appear to be a possible reason. The present state of quality assurance in Germany could certainly be improved, as non-adherence to guidelines is not currently followed by any relevant sanctions. In any case, the performance of PCI mainly for economic reasons, including the meeting of stated hospital objectives, clearly violates the code of medical ethics (39).

Overview

The selection of CCS patients for PCI must be more strictly bound to the recommendations of current guidelines, particularly in Germany. Current data show that PCI in addition to OMT in patients with CCS generally does not improve the clinical outcome. The quality of life is improved only in patients who have frequent angina pectoris.

For the time being, we can only say that, as knowledge grows, so does doubt (*Mit dem Wissen wächst der Zweifel* – J. W. Goethe).

Key messages

- In chronic coronary syndrome (CCS), the degree of stenosis seen on coronary angiography does not suffice for a functional assessment of coronary perfusion. The clinical relevance of a stenosis can only be judged with intracoronary test procedures or imaging techniques (stress echocardiography, stress MRI, SPECT, PET-CT).
- A percutaneous coronary intervention (PCI) performed only because of an angiographically demonstrated stenosis actually elevates the rate of myocardial infarction in all but a few patients and is therefore contraindicated. The degree of stenosis does, not in itself, permit any valid prognostication regarding the risk of myocardial infarction.
- No randomized trial has ever demonstrated that PCI in patients with CCS lowers either the infarction rate or the overall mortality, even if performed only for hemodynamically significant stenoses. PCI has been reported to improve the quality of life only in patients with frequent angina pectoris.
- The per capita rate of PCI in Germany is higher than anywhere else in Europe, and, unlike the rates in other countries, it is not declining. The selection of CCS patients for PCI needs to be more strictly bound to the recommendations of current guidelines, particularly in Germany.

Conflict of interest statement

Prof. Maier has served as a paid consultant for Berlin-Chemie, Gilead, and Mecavini. He has received lecture honoraria and reimbursement of meeting participation fees and travel expenses from Sanofi and Berlin-Chemie. He has also received third-party research funding from Gilead.

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