REVIEW

Early discharge compared with ordinary discharge after percutaneous coronary intervention – a systematic review and meta-analysis of safety and cost

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Aim: We aimed to summarize the pooled effect of early discharge compared with ordinary discharge after percutaneous coronary intervention (PCI) on the composite endpoint of re-infarction, revascularization, stroke, death, and incidence of rehospitalization. We also aimed to compare costs for the two strategies.

Methods: The study was a systematic review and a meta-analysis of 12 randomized controlled trials including 2962 patients, followed by trial sequential analysis. An estimation of cost was considered. Follow-up time was 30 days.

Results: For early discharge, pooled effect for the composite endpoint was relative risk of efficacy (RRe)=0.65, 95% confidence interval (CI) (0.52–0.81). Rehospitalization had a pooled effect of RRe=1.10, 95% CI (0.88–1.38). Early discharge had an increasing risk of rehospitalization with increasing frequency of hypertension for all populations, except those with stable angina, where a decreasing risk was noted. Advancing age gave increased risk of revascularization. Early discharge had a cost reduction of 655 Euros per patient compared with ordinary discharge.

Conclusion: The pooled effect supports the safe use of early discharge after PCI in the treatment of a heterogeneous population of patients with coronary artery disease. There was an increased risk of rehospitalization for all subpopulations, except patients with stable angina. Clinical trials with homogeneous populations of acute coronary syndrome are needed to be conclusive on this issue.

Keywords: percutaneous coronary intervention, early discharge, cost, meta-analysis

Introduction

Today, percutaneous coronary intervention (PCI) is one of the most commonly performed cardiac interventions.[1] The cost of treatment for acute coronary syndrome (ACS) in Western Europe is high and constitutes a considerable portion of total health care expenses. This is mainly attributed to revascularization procedures and the cost of hospital stay.[2,3]

Systematic use of stents and potent platelet inhibitors has revolutionized the success rate after PCI by drastically reducing the risk of acute occlusion in the first 24 hours after a successful procedure.[4] Reduced catheter sizes have made a transradial approach more feasible, which in turn has reduced bleeding incidents as well as the necessary observation time. Early discharge is routinely practiced in some parts of Europe and Canada but is rare in the US. Reasons may be concerns over patient safety and

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short-term clinical events, differences in procedures and use of pharmacology, as well as different systems for financial compensation.

With an increasing demand for hospital resources, the trend has moved toward the implementation of fast-track treatment pathways.[5] Several observational studies, and some randomized controlled trials (RCTs), have aimed to prove that same-day or early discharge after PCI is both feasible and safe. The patient populations in these studies include those with elective PCI, unstable angina pectoris (UAP), non-ST elevation myocardial infarction (NSTEMI), and ST elevation myocardial infarction (STEMI) patients.[6,7]

Cost analyses of early discharge versus ordinary discharge show that early discharge is economically favorable, primarily by eliminating the cost of overnight observation.[8–10]

Two meta-analyses and systematic reviews[11,12] claimed, based on observational studies and RCTs, support of programs for same-day discharge after PCI for selected groups of patients without defining the groups. The study populations in the RCTs that have been executed in this field are all relatively small. We have undertaken a systematic review and meta-analysis of only RCTs and have not considered observational studies.

The aim of this study was to summarize the pooled effect of early discharge compared with ordinary discharge after PCI on the primary composite endpoint of re-infarction, revascularization, stroke, death, and the incidence of rehospitalization. Second, we wanted to compare costs for the two strategies.

Methods

We searched the Cochrane Central Register of controlled trials (1970–2015), Embase (1980–2015), and Medline/PubMed (1966–2015). We combined the keywords outpatient, same day discharge, early discharge, percutaneous coronary intervention, PCI, angioplasty, economy, and cost. Similar strategies were used to search for previously published meta-analyses and reviews. We also screened reference lists and contacted authors. Our last update for research was done on August 5, 2015. No limitation on language was considered.

Inclusion criteria for the studies were RCTs comparing early discharge versus ordinary discharge after PCI and safety outcome data for up to 30 days following the index intervention, available for both groups separately. We included only studies from 1999 onward.

When cost analysis was available, it had to include an overview of cost related to both groups separately.

Twelve RCTs were considered eligible for this study (Figure 1).[4,13–23]

The definition of early discharge differs between the studies because of different patient populations. Eight studies have patients with stable coronary artery disease (CAD), UAP, and NSTEMI.[4,15–18,20,22,23] They define early discharge as discharge on the same day as the intervention. The remaining four studies have patients with STEMI.[13,14,19,21] Their definition of early discharge was discharge between 48 and 72 hours after the intervention.

Three of these included an analysis of cost.[20,22,23] Two additional articles with an assessment of cost were based on studies already included in the safety analysis, and we added these to our cost analyses.[8,9] Andersen et al[16] originally included 399 patients in their study. In the meta-analysis of safety, we have considered only the 167 who had PCI during their index stay.

Endpoints

Our primary endpoint was the incidence of the composite cardiovascular events mortality, re-infarction, revascularization, and stroke. The secondary endpoint was rehospitalization, both endpoints within 30 days after PCI. Finally, a 30-day estimation of the cost of the two strategies was considered.

The statistical methods used for our analyses have previously been described in detail by Abdelnoor et al.[24]
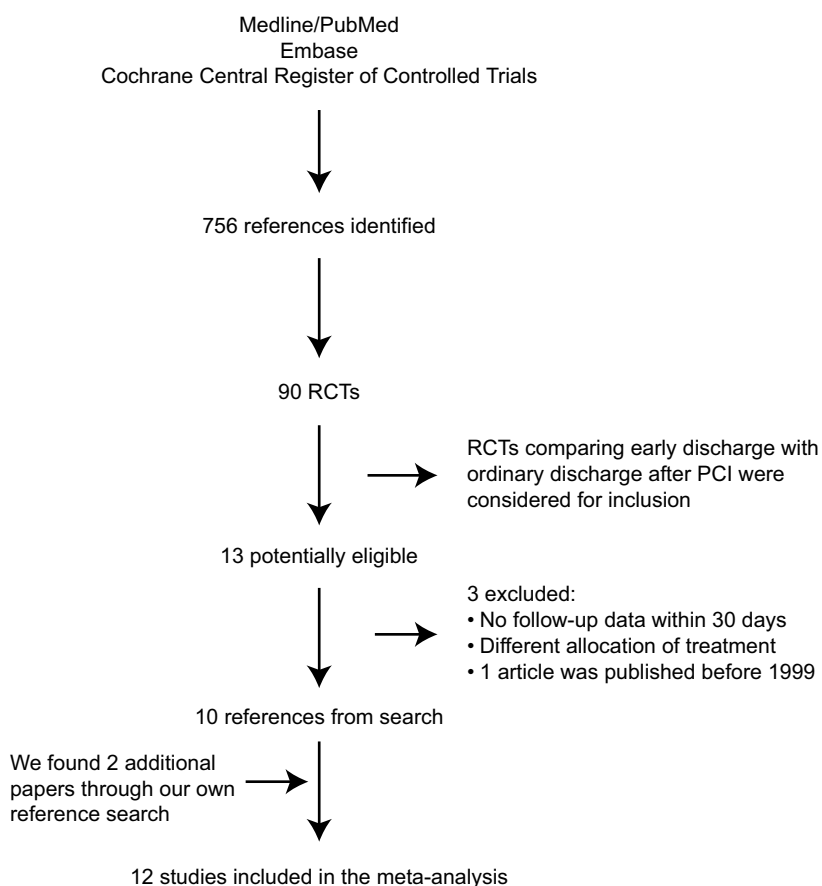
Trial sequential analysis (TSA) was used according to Pogue and Yusuf[25] and Wetterslev et al.[26] We used TSA as it is implemented in the STATA Program 12 (StataCorp LLC, College Station, TX, USA). This method permits to consider the accumulated number of patients to estimate the power of our cumulative meta-analysis.

Robustness of the pooled estimates was checked by sensitivity analysis. Each of the studies was individually omitted from the data set, followed in each case by recalculation of the pooled estimate of the remaining studies.

We followed the PRISMA guidelines for meta-analyses and systematic reviews of randomized trials in this report.[27]

Results

The baseline characteristics are represented in Table 1. The 12 trials included 2962 patients, 1486 patients in the early discharge group and 1476 patients in the ordinary discharge group. Considering the study-level variables with regard to the primary endpoint, 37% had concealment of randomization, 27% had outcome blinded to the investigators, 91%

Medline/PubMed
Embase
Cochrane Central Register of Controlled Trials

↓

756 references identified

↓

90 RCTs

→ RCTs comparing early discharge with ordinary discharge after PCI were considered for inclusion

↓

13 potentially eligible

→ 3 excluded:
• No follow-up data within 30 days
• Different allocation of treatment
• 1 article was published before 1999

↓

10 references from search

We found 2 additional papers through our own reference search →

↓

12 studies included in the meta-analysis

Figure 1 Details of the search process. Last search was performed August 5, 2015.
Abbreviations: RCTs, randomized controlled trials; PCI, percutaneous coronary intervention.

Table 1 Baseline characteristics

Characteristics	References											
	Azzalini et al[13] (n=100)	Melberg et al[14] (n=215)	Kim et al[15] (n=298)	Falcone et al[17] (n=44)	Bertrand et al[18] (n=1005)	Kotowycz et al[19] (n=54)	Glaser et al[20] (n=39)	Jirmar et al[21] (n=56)	Heyde et al[22] (n=800)	Carere et al[23] (n=100)	Andersen et al[16] (n=167)	Knopf et al[4] (n=90)
UAP, n	0	0	0	0	482	0	0	0	75	50	34	38
NSTEMI, n	0	0	0	0	188	0	0	0	0	0	133	0
STEMI, n	100	215	0	0	335	54	0	56	0	0	0	0
Stable AP, n	0	0	298	44	0	0	39	0	725	50	0	52
Age, mean	59.2	–	55.9	59	60.5	55.3	61	56.7	61.6	60.5	66	58
Female %	14	13.5	26	29.5	21.4	25.9	5	41.1	19	17	25	37
Diabetes %	12	7.9	49.3	45.5	16	22.5	33	23.4	15	–	22	20
Hypertension %	44	29.8	–	90.9	53.5	44.5	77	41.2	40	–	53	56
Prior MI %	4	6.5	–	25	44.1	–	31	0	36	–	27	31
Prior PCI %	4	5.6	–	45.4	19.9	–	56	–	21	–	34	47
Prior CABG %	0	0.5	–	–	–	–	10	–	4	–	8	13
Femoral access %	9	41.4	66.4	100	0	–	100	100	100	100	11.8	100

Abbreviations: –, unknown; UAP, unstable angina pectoris; NSTEMI, non-ST elevation myocardial infarction; STEMI, ST elevation myocardial infarction; AP, angina pectoris; prior MI, prior myocardial infarction; prior PCI, prior percutaneous coronary intervention; prior CABG, prior coronary artery bypass graft.

used the intention-to-treat analysis, and 81% of the trials did not have drop-out during follow-up. For the outcome rehospitalization, 36% had concealment of randomization, 27% had blinding of the investigators to the outcome, 91%

used the intention-to-treat analysis, and 82% of the trials did not have drop-out during follow-up.

The majority of the trials suffered serious methodological biases and were power deficient. Five RCTs included

cost analysis and were included in the cost study. Three of these had correct concealment, one had blinding of investigator to the outcome, four followed the intention-to-treat analysis, and three had no drop-out during follow-up. All costs were recalculated to the value of the Euro in December 2014.

Primary composite endpoint

The pooled estimate of the efficacy (Tables 2 and 3) showed an estimate of relative risk [RR]=0.65, 95% confidence interval (95% CI) (0.52–0.81), p=0.0002, indicating a lower risk in the early discharge group compared to ordinary discharge group for the primary composite endpoint with no heterogeneity. There was no selection bias. We ran subgroup and meta-regression analyses on study-level and patient-level variables. Meta-regression is a method to investigate heterogeneity, and it permits to quantify the association between variables and effect of the intervention. With regard to study-level variables, none was associated with the efficacy. Considering patient-level variables, none of the covariates showed an association with the efficacy on the primary endpoint (Tables 2 and 3).

A sensitivity analysis revealed the non-robustness of our results for the primary composite endpoint. Our hypothesis was a risk reduction of 15% lower incidence in the ordinary care group versus early discharge group. For an accumulated number of 2912 patients and a type I error of 5%, we have a power of the cumulative meta-analysis of 98%. For the primary composite endpoint, our meta-analysis includes enough patients and has satisfactory power.

Re-infarction and rehospitalization

Another run of pooled efficacy and sensitivity analysis on re-infarction and incidence of revascularization showed that for re-infarction the pooled RR of efficacy

Table 2 Pooled estimate of RR of efficacy for ED compared to OC on the primary composite endpoint, with stratification on attrition bias and detection bias using the fixed-effect model

Subdivision	Studies (n)	RRe (95% CI)	Tau²	I², %	p-valueᵃ
All studies	11	0.65 (0.52–0.81)	0.00	0.0	0.0002
No drop-out					
Yes	9	0.73 (0.46–1.18)	0.0000	0.0	0.5581
No/unclear	2	0.73 (0.46–1.18)	0.0001	0.0	
Investigator blind to the outcome					
Yes	2	0.62 (0.48–0.80)	0.0000	0.0	0.4785
No	9	0.75 (0.47–1.18)	0.000	0.0	

Notes: Tau²: inter-study variability. ᵃTest for subgroup differences using random-effect model between groups with Q statistics df=1 and p-value. Data adapted from references 4, 13–18, and 20–23.
Abbreviations: RRe, relative risk of efficacy; ED, early discharge; OC, ordinary care; CI, confidence interval.

Table 3 Estimate of the mixed-effect regression model between logRR and primary composite endpoint and the different study-level and patient-level variables in a univariate analysis using 11 trials

| Covariates	Level	β-coefficient	Std err (β)	Z	P-value
Publication year	Years	−0.0305	0.0886	−0.34	0.7304
Concealment	Yes/no	0.5152	0.9178	0.56	0.5745
Blinding investigator	Yes//no	−0.1885	0.2659	−0.70	0.4785
No drop-out	Yes/no	0.1600	0.2731	0.58	0.5581
ITT analysis	Yes/no	−0.8105	0.8355	0.97	0.3320
Age of the patient	Years	0.0363	0.1688	0.21	0.8298
Female	Percentage	0.0179	0.0218	0.82	0.4100
Diabetes	Percentage	0.0165	0.0541	0.30	0.7595
Hypertension	Percentage	0.0167	0.0189	0.88	0.3744
STEMI	Percentage	0.0019	0.0069	0.27	0.7838
NSTEMI or UAP	Percentage	0.0039	0.0044	0.89	0.3739
Stable AP	Percentage	−0.0021	0.0039	−0.17	0.4776

Note: Data adapted from references 4, 13–18, and 20–23.
Abbreviations: RR, relative risk; Std err, standard error; ITT, intention-to-treat analysis; STEMI, ST elevation myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; UAP, unstable angina pectoris; AP, angina pectoris.

was RR=0.45, 95% CI (0.31–0.66), p=0.001, for early discharge compared to ordinary discharge, with no heterogeneity considering 10 studies. A sensitivity analysis confirmed the non-robustness of our results with regard to re-infarction. With regard to revascularization, we found a pooled efficacy of RR=0.38, 95% CI (0.18–0.79), p=0.009, for early discharge compared to ordinary discharge. A sensitivity analysis pinpointed the non-robustness of our results. Meta-regression showed a significant increase of risk for revascularization in the early discharge group with increasing prevalence of NSTEMI/UAP (Figure 2) and the same with increasing age of the patient. With increasing prevalence of stable angina, there was a decreasing risk of revascularization in the early discharge group compared with ordinary discharge (Figure 3).

Endpoint rehospitalization

The pooled estimate of the effect of the early discharge showed an estimate of RR=1.10, 95% CI (0.88–1.38), p=0.37, with a substantial heterogeneity of 16% with no difference of efficacy in the two groups, There was no selection bias. A sensitivity analysis using the random model indicated the non-robustness of our results. We ran a subgroup analysis (Table 4) and meta-regression (Table 5) on study-level and patient-level variables. Regarding study-level variables, concealment (p=0.004), blinding (p=0.001), and drop-out
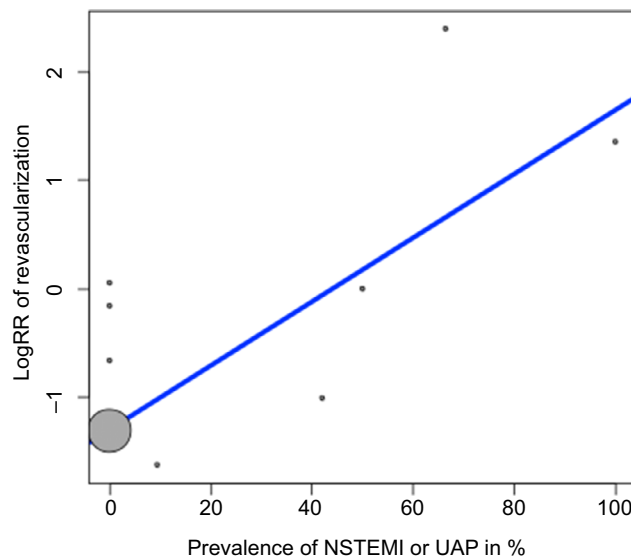
Figure 2 Meta-regression for the efficacy of ED compared to OD on the incidence of revascularization versus prevalence of NSTEMI or UAP
Notes: The size of the circles is an indicator of the size of the trial. Data adapted from references 4, 13–16, 18, 20, 21, and 23.
Abbreviations: ED, early discharge; OD, ordinary discharge; NSTEMI, non-ST elevation myocardial infarction; UAP, unstable angina pectoris; RR, relative risk.
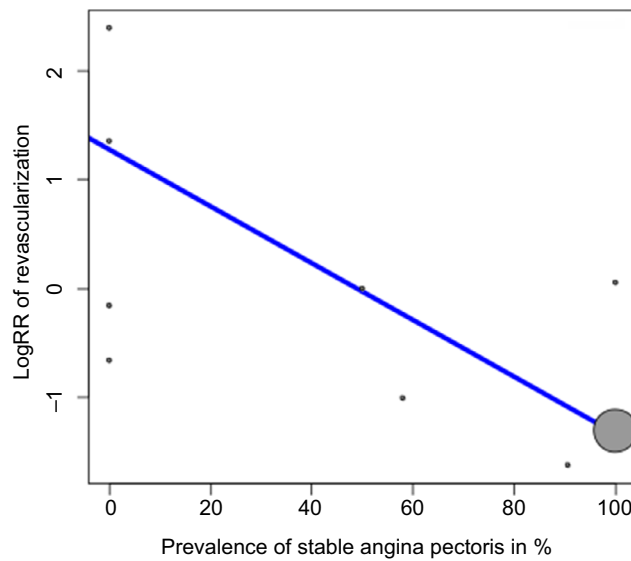
Figure 3 Meta-regression for the efficacy of ED compared to OD on the incidence of revascularization versus prevalence of stable angina pectoris.
Notes: The size of the circles is an indicator of the size of the trial. Data adapted from references 4, 13–16, 18, 20, 21, and 23.
Abbreviations: ED, early discharge; OD, ordinary discharge; RR, relative risk.

(p=0.004) during follow-up were associated with efficacy, as also the prevalence of STEMI (p=0.005), NSTEMI/UAP (p=0.001), and stable angina (p=0.008). This indicates an association between efficacy of early discharge and those variables.

For the patient-level variables, the frequency of hypertension was associated with efficacy (p=0.004) (Figure 4). This indicates increasing risk of rehospitalization for patients in the early discharge group compared to the

Table 4 Pooled estimate of RR of efficacy for ED compared to OD on the endpoint rehospitalization, with stratification on concealment and no drop-out using the random-effect model

Subdivision	Studies (n)	RRe (95% CI)	Tau²	I², %	p-valueª
All studies	12	1.10 (0.88–1.38)	0.0191	16	0.3713
Concealment					
Yes	4	0.88 (0.71–1.10)	0	0	0.0039
No/Unclear	8	1.34 (1.13–1.61)	0	0	
No drop-out during follow-up					
Yes	10	1.34 (1.13–161)	0.2382	21.6	0.5868
No	2	1.04 (0.41–2.61)	0	0	

Notes: Tau²: inter-study variability. ªTest for subgroup differences using random-effect model between groups with Q statistics df=1 and p-value. Data adapted from references 4 and 13–23.
Abbreviations: RRe, relative risk of efficacy; ED, early discharge; OD, ordinary discharge; CI, confidence interval.

Table 5 Estimate of the mixed-effect regression model between logRR and rehospitalization and the different study-level and patient-level variables in a univariate analysis using 12 trials

| Covariates	Level	β-coefficient	Std err (β)	Z	p-value
Publication year	Years	−0.0178	0.0491	−0.36	0.7170
Concealment	Yes/no	−0.4184	0.1449	−2.88	0.0039
Blinding investigator	Yes/no	−0.4706	0.1431	−3.28	0.0010
No drop-out	Yes/no	0.4194	0.1451	2.89	0.0038
ITT analysis	Yes/no	−1.2674	1.3266	−0.95	0.3339
Age of the patient	Years	0.0596	0.0820	0.72	0.4674
Female	Percentage	0.0189	0.0444	0.4259	0.6701
Diabetes	Percentage	−0.0084	0.0127	−0.66	0.5091
Hypertension	Percentage	0.0297	0.0102	2.91	0.0036
STEMI	Percentage	0.0100	0.0036	2.81	0.005
NSTEMI or UAP	Percentage	0.0079	0.0024	3.28	0.0010
Stable AP	Percentage	−0.0052	0.0016	−3.25	0.008

Note: Data adapted from references 4 and 13–23.
Abbreviations: RR, relative risk; Std err, standard error; ITT, intention-to-treat analysis; STEMI, ST elevation myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; UAP, unstable angina pectoris; AP, angina pectoris.

ordinary care group with increasing frequency of hypertension, increasing prevalence of STEMI, and increasing prevalence of NSTEMI/UAP. There was a decreasing risk for rehospitalization with increasing prevalence of stable angina (Figure 5).

The TSA for the endpoint rehospitalization had a hypothesis of 15% risk reduction for rehospitalization in the ordinary discharge group compared to the early discharge group. For an accumulated number of 2912 patients and a type I error of 5%, we have a power of the cumulative meta-analysis of 92%.

We can conclude that for the endpoint rehospitalization, our cumulative meta-analysis has satisfactory power.
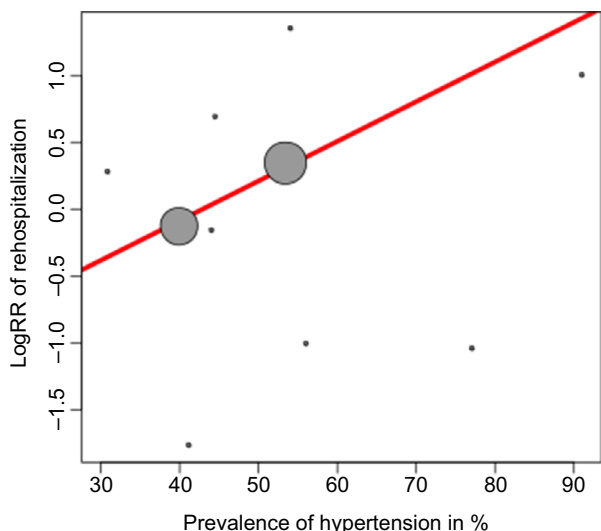
Figure 4 Meta-regression for the efficacy of ED compared to OD on the incidence of rehospitalization versus prevalence of hypertension.
Notes: The size of the circles is an indicator of the size of the trial. Data adapted from references 4, 13, 14, and 16–22.
Abbreviations: ED, early discharge; OD, ordinary discharge; RR, relative risk.
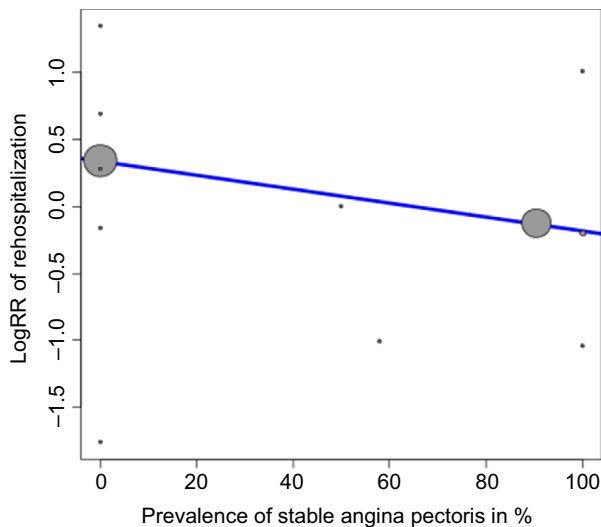
Figure 5 Meta-regression of the efficacy of ED compared to OD on the incidence of rehospitalization versus prevalence of stable angina pectoris
Notes: The size of the circles is an indicator of the size of the trial. Data adapted from references 4 and 13–23.
Abbreviations: ED, early discharge; OD, ordinary discharge; RR, relative risk.

Cost

We identified five RCTs that described the economic impact related to early discharge compared with ordinary discharge after PCI (Table 6).[8,9,20,22,23] Most of the studies separated procedural cost and the cost of care and observation after the intervention. Three studies described total costs. Three articles mentioned only the cost of care and observation and estimated that procedural costs would be the same in both groups. One study calculated with larger procedural cost in the early discharge group due to the use of a vascular closure device. Rehospitalization within the follow-up period was included in the costs.

Table 6 Cost between the two strategies ED and OD after PCI (Euros per patient)

Reference	Year for calculation	ED procedure cost	Non-procedure ED cost	ED total cost	ED LOS (hours)	OD procedure cost	Non-procedure OD cost	Total OD cost	OD LOS (hours)	Total OD cost vs total ED cost
Andersen et al (2016),[9] n=167*	2010	2328	483	2856	5.90	2377	884	3391	29.79	535 (15.8%)
Rinfret et al (2010),[8] n=1005	2006	–	915	–	8.9	–	1850	–	26.5	935 (50.5%)
Glaser et al (2000),[20] n=39	2006	–	–	8227	–	–	–	10102	–	1875 (18.6%)
Heyde et al (2007),[22] n=800	2003	–	–	5615	–	–	–	5925	–	310 (5.2%)
Carere et al (2000),[23] n=100**	1998	–	453	–	11.5	–	747	–	26.49	294 (39.4%)

Notes: Costs and LOS are mean values and include index and 30 days follow-up. *Andersen et al included index and 30 days follow-up. We have included the 167 who had PCI on their index stay. **3 days follow-up.
Abbreviations: –, unknown; ED, early discharge; OD, ordinary discharge; PCI, percutaneous coronary intervention; LOS, length of stay.

All studies found a decrease in total treatment cost for the early discharge group, with a reduction of 5.2%–50.1%. In these studies, this means a saving of 294–1875 Euros per patient.

Three studies disclosed the length of stay (LOS).[8,9,23] LOS included the index stay as well as subsequent rehospitalization within 30 days. Mean LOS varied between 5.9 hours in the early discharge group to 29.8 hours in the ordinary care group.

Discussion
Safety

The results of our systematic review indicated a reduction in the composite clinical endpoint with early discharge. However, there was a possibility of increased risk of rehospitalization for early discharge compared to ordinary care patients with hypertension and an increasing risk of UAP/revascularization with increasing age of the patient.

Our results regarding the safety of early discharge compared to ordinary care on the outcomes of the primary and secondary endpoints changed when we arranged the components of trial quality. The trials were assessed individually and methodologically, and their influence on effect size was explored. It has been shown that when studies of low methodological quality are incorporated into the meta-analysis, the estimate of quality can alter the interpretation of the benefit of the intervention. We found a reduction in the primary composite endpoint for the early discharge strategy. We found a possibility of increasing risk of rehospitalization with early discharge with increasing frequency of hypertension.

When heterogeneity was present, we performed meta-regression analyses on study-level and patient-level variables. It was not performed if the number of studies was <10. We had specified patient-level variables a priori in the protocol of our meta-analysis. Only biologically plausible mechanisms were considered.[28,29]

Patient-related variables such as frequency of hypertension and age of patients can be subject to ecological fallacy and should be considered hypothesis generating,[30] while the study-level variables that were considered in this meta-regression (concealment of randomization, drop-out) can detect real associations between effect of the treatment and the study-level variables.[31]

Our results show that unstable patients are more often the subject of complications and rehospitalization. Increasing age often results in co-morbidities and a higher risk. An unexpected finding was that the prevalence of hypertension should mean increased risk for rehospitalization. This indicates that extra care must be taken to assess risk and in selecting the appropriate patients suitable for early discharge.

Cost

Procedural variables are the strongest predictor of post-procedural complications.[32] Vavalle et al[33] found that the patients with longer LOS often had more co-morbidities and in-hospital complications. Analyzing procedural results can help triage patients suitable for early discharge. The use of validated risk scores such as Zwolle can be of help in identifying low-risk patients, suitable for early discharge.[34] The decrease in costs in the early discharge group is due to the reduction in LOS, and thus in the cost of care, both at the index stay and in the days of follow-up. This is confirmed by Le Corvoisier et al.[35]

Bakhai et al[3] found that the risk of a new clinical event within 1 year after ACS treated with PCI is high among the Western European population. A finding of Korsnes et al[36] was that the first major adverse cardiovascular event is more costly than subsequent events. Several studies have found that most adverse events related to the intervention occur shortly post-procedure and not in an extended observational period.[37–39] This is in line with the results of the studies included in this meta-analysis and also with our pooled results. This suggests that occurrence of adverse events is not related to the discharge procedure. It is thus possible to decrease direct expenses by reducing LOS, considering the specific diagnosis of the patient. Our results show an increased risk of rehospitalization in the early discharge group, with the exception for patients with stable angina. Despite this finding, we see a reduction of cost in the early discharge group.

The time allotted to an intervention is the same, regardless of discharge strategy. Early discharge does not free up resources in the laboratory itself. But by reduced LOS in the early discharge group, resources used for observation and monitoring of patients were made available. Unfortunately, none of the studies in our meta-analysis have explored in what way these additional resources have been utilized or in what way this affects the economy.

A limitation to this cost analysis is that not all studies disclose the total cost. The reporting of costs included is also of variable quality. We have looked at costs related to the population as a whole because the quantitative basis for differentiating between STEMI, NSTEMI, UAP, and elective procedures is too small. It is possible that cost-effectiveness may vary between the groups to a greater extent than shown here.

Strengths and limitations

The major limitations of our study were the use of heterogeneous patient populations, quality of the trials with respect

to the effect estimated, heterogeneity, underpowered trials, and use of other endpoints than our primary endpoint and rehospitalization.

Conclusion

Expenses in the early discharge group were lower compared with the ordinary discharge group, mainly due to a reduction in LOS and the cost of care.

The pooled effect for the composite cardiovascular endpoint supports the safe use of early compared to ordinary discharge after PCI in the treatment of a heterogeneous population of patients with CAD. However, for the endpoint rehospitalization, an increased risk was noted in patients with STEMI, NSTEMI, or unstable angina, but not in patients with stable angina.

Clinical trials with homogeneous populations of ACS are needed to be conclusive on this issue.

Disclosure

The authors report no conflicts of interest in this work.

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