Quality of Life After Treatment of Chronic Total Occlusions with Revascularization versus Optimal Medical Therapy

Werner GS, Martin-Yuste V, Hildick-Smith V, et al; EUROCTO trial investigators. A randomized multicentre trial to compare revascularization with optimal medical therapy for the treatment of chronic total coronary occlusions. Eur Heart J. 2018;39:2484-2493.

Study Overview

Objective. To compare the benefit of percutaneous coronary intervention (PCI) plus optimal medical therapy (OMT) versus OMT alone on the health status of patients with chronic total occlusions (CTOs).

Design. Multicenter, open-label, prospective randomized control trial.

Setting and participants. 396 patients with at least 1 CTO were assigned to PCI or OMT with a 2:1 randomization ratio.

Main outcome measures. The primary endpoint was the change in health status as assessed by the Seattle Angina Questionnaire (SAQ) between baseline and 12-month follow-up.

Main results. At 12 months, greater improvement of 3 SAQ domains was observed with PCI compared to OMT: angina frequency (5.23, 95% confidence interval [CI], 1.75-8.31, $P = 0.0003$), physical limitation ($P = 0.02$), and quality of life (6.62, 95% CI 1.78-11.46, $P = 0.0007$). More patients in the PCI group than in the OMT group had complete freedom from angina (71.6% vs. 57.8%, $P = 0.008$). There were no occurrences of periprocedural death or myocardial infarction.

Conclusion. Among patients with stable angina and CTO, PCI leads to significant health status improvement compared with OMT alone.

Commentary

CTOs are present in 15% to 25% of patients undergoing coronary angiogram[1] and are associated with increased mortality.[2] The benefits of successful CTO intervention observed in multiple large-scale registries include improvement in quality of life, left ventricular function, and survival as well as avoidance of coronary bypass surgery. The main indication for CTO intervention is improvement in quality of life,[3] although this has not been confirmed by a randomized controlled trial comparing medical therapy to CTO-PCI.

Previous studies have assessed the health status ben-

efits associated with CTO-PCI.[4,5] Most recently, the OPEN CTO study showed significant improvement in health status in 1000 consecutive patients undergoing CTO-PCI in 12 experienced U.S. centers.[6] Similarly, in a Canadian registry, revascularization of CTO was associated with greater health status benefit compared to medical therapy alone.[4] However, these studies compared CTO-PCI success to failure, rather than to medical therapy.

In this context, Werner and colleagues investigated the value of PCI versus OMT for CTO by performing a well-designed randomized clinical trial in patients with CTO by assessing their health status with the SAQ.[7] The SAQ is a 19-item questionnaire with a 4-week recall period that measures 5 domains of health status in patients with coronary artery disease (CAD).[8,9] Scores in each domain range from 0 to 100, with higher scores indicating fewer symptoms and better quality of life. The SAQ has undergone extensive reliability and validity testing and is associated with long-term survival and health care utilization among patients with chronic CAD.[10,11] At 12 months follow-up, patients who underwent CTO-PCI had greater improvement in SAQ subscales, including angina frequency and quality of life, reaching the pre-specified significance level of 0.01. There was also numerical improvement in physical limitation ($P = 0.02$)

The strengths of this current study include the randomized design and the careful treatment of non-CTO-PCI lesions before enrollment into the study. These non-CTO lesions were treated before the baseline health status assessment so that the additional health status benefit of non-CTO-PCI would not affect the results. This was one of multiple major limitations of the recently presented DECISION-CTO trial, as the non-CTO lesions were treated after the randomization and baseline assessment, leading to inaccurate comparison between medical therapy and CTO-PCI.[12]

Another interesting point of the current study is the patient selection. Since the treatment sites included were all expert centers in Europe, many patients who were referred to their institution for CTO-PCI were excluded from the study. For example, among the 1980 patients with screening log, 1381 were excluded because they were referred for CTO-PCI and 122 were excluded because they were "too symptomatic." This suggests that the population studied were less symptomatic than the overall symptomatic CTO population from previous registries, as evidenced by about 40% of patients having Canadian Cardiovascular Society (CCS) class I/II angina at baseline. In the recent consecutively enrolled OPEN CTO registry, only 26% of patients reported CCS class I/II angina at baseline.[6] These observations likely represent biases to the null, and thus one can reasonably speculate that the impact among unselected patients would be greater. Degree of baseline angina has been reported to be a predictor in patients with stable angina.[13] Moreover, the degree of health status improvement is significantly larger in patients with refractory angina undergoing CTO- PCI.[14]

In this study, the success rate of CTO PCI was 83.1% at the initial attempt and 86.6% at the final attempt. The in-hospital complication rate was 2.9%, which included pericardial tamponade, vascular surgical repair, and need for blood transfusion. The success rate and complication rates were consistent with previous observational studies from expert centers.[1,6]

Applications for Clinical Practice

In patients presenting with stable angina with CTO, the health status improvement is larger with CTO-PCI plus medical therapy compared to medical therapy alone. CTO-PCI should be offered to symptomatic patients in conjunction with OMT.

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References

1. Fefer P, Knudtson ML, Cheema AN, et al. Current perspectives on coronary chronic total occlusions: the Canadian Multicenter Chronic Total Occlusions Registry. *J Am Coll Cardiol.* 2012;59:991-997.
2. Ramunddal T, Hoebers LP, Henriques JP, et al. Prognostic impact of chronic total occlusions: a report from SCAAR (Swedish Coronary Angiography and Angioplasty Registry). *JACC Cardiovasc Interv.* 2016;9:1535-1544.
3. Grantham JA, Marso SP, Spertus J, et al. Chronic total occlusion angioplasty in the United States. *JACC Cardiovasc Interv.* 2009;2:479-486.
4. Wijeysundera HC, Norris C, Fefer P, et al. Relationship between initial treatment strategy and quality of life in patients with coronary chronic total occlusions. *EuroIntervention.* 2014;9:1165-1172.
5. Grantham JA, Jones PG, Cannon L, Spertus JA. Quantifying the early health status benefits of successful chronic total occlusion recanalization: Results from the FlowCardia's Approach to Chronic Total Occlusion Recanalization (FACTOR) Trial.

Circ Cardiovasc Qual Outcomes. 2010;3:284-290.
6. Sapontis J, Salisbury AC, Yeh RW, C et al. Early procedural and health status outcomes after chronic total occlusion angioplasty: a report from the OPEN-CTO registry (Outcomes, Patient Health Status, and Efficiency in Chronic Total Occlusion Hybrid Procedures). *JACC Cardiovasc Interv.* 2017;10:1523-1534.
7. Werner GS, Martin-Yuste V, Hildick-Smith D, et al. A randomized multicentre trial to compare revascularization with optimal medical therapy for the treatment of chronic total coronary occlusions. *Eur Heart J.* 2018;39:2484-2993.
8. Spertus JA, Winder JA, Dewhurst TA, et al. Monitoring the quality of life in patients with coronary artery disease. *Am J Cardiol.* 1994;74:1240-1244.
9. Spertus JA, Winder JA, Dewhurst TA, et al. Development and evaluation of the Seattle Angina Questionnaire: a new functional status measure for coronary artery disease. *J Am Coll Cardiol.* 1995;25:333-341.
10. Mozaffarian D, Bryson CL, Spertus JA, et al. Anginal symptoms consistently predict total mortality among outpatients with coronary artery disease. *Am Heart J.* 2003;146:1015-1022.
11. Spertus JA, Jones P, McDonell M, et al. Health status predicts long-term outcome in outpatients with coronary disease. *Circulation.* 2002;106:43-49.
12. Park S. Drug-eluting stent versus optimal medical therapy in patients with coronary chronic total occlusion: DECISION CTO randomized trial. Presented at the American College of Cardiology Annual Scientific Session (ACC 2017), Washington, DC, March 18, 2017.
13. Spertus JA, Salisbury AC, Jones PG, et al. Predictors of quality-of-life benefit after percutaneous coronary intervention. *Circulation.* 2004;110:3789-3794.
14. Hirai T, Grantham JA, Gosch K, L et al. Quality of life in patients with refractory angina after chronic total occlusion angioplasty. *J Am Coll Cardiol.* 2018;72(13 supplement):TCT-79.

Effectiveness of Epinephrine in Out-of-Hospital Cardiac Arrest

Perkins GD, Ji C, Deakin CD, et al. A randomized trial of epinephrine in out-of-hospital cardiac arrest. N Engl J Med. 2018;379:711-721.

Study Overview

Objective. To assess the safety and effectiveness of the use of epinephrine in out-of-hospital cardiac arrest patients.

Design. Randomized, double-blind placebo-controlled trial in the United Kingdom.

Setting and participants. Patients aged 16 years or older who had sustained an out-of-hospital cardiac arrest for which advanced life support was provided by trial-trained paramedics were eligible for inclusion. Exclusion criteria included apparent pregnancy, arrest from anaphylaxis or asthma, or the administration of epinephrine before the arrival of the trial-trained paramedic. In 1 of the 5 ambulance services, traumatic cardiac arrests were also excluded in accordance with local protocol.

Main outcome measures. The primary outcome was the rate of survival at 30 days. Secondary outcomes included rate of survival until hospital admission, length of stay in the hospital and intensive care unit (ICU), rates of survival at hospital discharge and at 3 months, and neurologic outcomes at hospital discharge and at 3 months.

Main results. Between December 2014 and October 2017, 10,623 patients were screened for eligibility in 5 National Health Service ambulance services in the United Kingdom. Of these, 8103 were eligible, and 8014 patients were assigned to either the epinephrine group (4015 patients) or the placebo group (3999 patients).

For the primary outcome, 130 patients (3.2%) in the epinephrine group were alive at 30 days in comparison to 94 patients (2.4%) in the placebo group (unadjusted odds ratio [OR] for survival, 1.39; 95% confidence interval [CI], 1.06-1.82; $P = 0.02$). The number needed to treat for a 30-day survival was 112 patients (95% CI, 63-500).

For the secondary outcomes, the epinephrine group had a higher survival until hospital admission: 947 patients (23.8%) as compared to 319 (8.0%) patients in the placebo group (unadjusted OR, 3.59). Otherwise, there were no difference between the 2 groups in the hospital and ICU LOS. There also was not a significant difference

between the epinephrine group and the placebo group in the proportion of patients who survived until hospital discharge: 87 of 4007 patients (2.2%) in the epinephrine group and 74 of 3994 patients (1.9%) in the placebo group, with an unadjusted OR of 1.18 (95% CI, 0.85-1.61). Patients in the epinephrine group had a higher rate of severe neurologic impairment at discharge: 39 of 126 patients (31.0%) versus 16 of 90 patients (17.8%).

Conclusion. Among adults with out-of-hospital cardiac arrest, the use of epinephrine resulted in a higher rate of 30-day survival as compared with the use of placebo; however, there was no difference in the rate of a favorable neurologic outcome as more survivors in the epinephrine group had severe neurologic impairment.

Commentary

Epinephrine has been used as part of the resuscitation of patients with cardiac arrest since the 1960s. Epinephrine increases vasomotor tone during circulatory collapse, shunts more blood to the heart, and increases the likelihood of restoring spontaneous circulation.[1] However, epinephrine also decreases microvascular blood flow and can result in long-term organ dysfunction or hypoperfusion of the heart and brain.[2] The current study, the PARAMEDIC2 trial, by Perkins and colleagues is the largest randomized controlled trial to date to address the question of patient-centered benefit of the use of epinephrine during out-of-hospital cardiac arrest.

Similar to prior studies, patients who received epinephrine had a higher rate of 30-day survival than those who received placebo. However, there was no clear improvement in functional recovery among patients who survived, and the proportion of survivors with severe neurologic impairment was higher in the epinephrine group as compared to the placebo group. These results demonstrate that despite its ability to restore spontaneous circulation after out-of-hospital cardiac arrest, epinephrine produced only a small absolute increase in survival with worse functional recovery as compared with placebo.

One major limitation of this study is that the protocol did not control for or measure in-hospital treatments. In a prior study, the most common cause of in-hospital death was iatrogenic limitation of life support, which may result in the death of potentially viable patients.[3] Another limitation of the study was the timing to administration of epinephrine. In the current study, paramedics administered the trial agent within a median of 21 minutes after the emergency call, which is a longer duration than previous out-of-hospital trials.[4] In addition, this time to administration is much longer than that of in-hospital cardiac arrest, where epinephrine is administered a median of 3 minutes after resuscitation starts.[5] Therefore, the results from this study cannot be extrapolated to patients with in-hospital cardiac arrest.

Applications for Clinical Practice

The current study by Perkins et al demonstrated the powerful effect of epinephrine in restoring spontaneous circulation after out-of-hospital cardiac arrest. However, epinephrine produced only a small absolute increase in survival with worse functional recovery, as compared to placebo. While further studies regarding dosage of epinephrine as well as administration based on the basis of cardiac rhythm are needed, we should question our tradition of using epinephrine in out-of-hospital cardiac arrest if meaningful neurological function is our priority.

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References

1. Paradis NA, Martin GB, Rosenberg J, et al. The effect of standard-ad high-dose epinephrine on coronary perfusion pressure during prolonged cardiopulmonary resuscitation. *JAMA.* 1991;265:1139-1144.
2. Ristagno G, Sun S, Tang W, et al. Effects of epinephrine and vasopressin on cerebral microcirculatory flows during and after cardiopulmonary resuscitation. *Crit Care Med.* 2007;35:2145-2149.
3. Elmer J, Torres C, Aufderheide TP, et al. Association of early withdrawal of life-sustaining therapy for perceived neurological prognosis with mortality after cardiac arrest. *Resuscitation.* 2016;102:127-135.
4. Kudenchuk PJ, Brown SP, Daya M, et al. Amiodarone, lidocaine, or placebo in out-of-hospital cardiac arrest. *N Engl J Med.* 2016;374:1711-1722.
5. Donnino MW, Salciccioli JD, Howell MD, et al. Time to administration of epinephrine and outcome after in-hospital cardiac arrest with non-shockable rhythms: retrospective analysis of large in-hospital data registry. *BMJ.* 2014;348:g3028l.

Bundled Hospital-at-Home and Transitional Care Program Is Associated with Reduced Rate of Hospital Readmission

Federman AD, Soones T, DeCherrie LV, et al. Association of a bundled hospital-at-home and 30-day postacute transitional care program with clinical outcomes and patient experiences. JAMA Intern Med. 2018;178:1033-1040.

Study Overview

Objective. To examine the effect of a hospital-at-home (HaH) and transitional care program on clinical outcomes and patient experiences when compared with inpatient hospitalization.

Design. Cohort study with matched controls.

Setting and participants. The study was conducted in a single center and aimed to evaluate a HaH program bundled with a 30-day postacute period of home-based transitional care. The program is funded by the Center for Medicare and Medicaid Innovation of the Centers for Medicare and Medicaid Services (CMS) with the goal of establishing a new HaH program that provides acute hospital-level care in a patient's home as a substitute for transitional inpatient care.

Patients were eligible for the program if they were aged 18 years or older, lived in Manhattan, New York, had fee-for-service Medicare or private insurer that had contracted for HaH services, and required inpatient hospital admission for eligible conditions. Eligible conditions included acute exacerbations of asthma or chronic obstructive pulmonary disease, congestive heart failure (CHF), urinary tract infections (UTI), community-acquired pneumonia (CAP), cellulitis of lower extremities, deep venous thrombosis, pulmonary embolism, hypertensive urgency, hyperglycemia, and dehydration; this list was later expanded to 19 conditions representing 65 diagnosis-related groups. Patients were excluded if they were clinically unstable, required cardiac monitoring or intensive care, or lived in an unsafe home environment. Patients were identified in the emergency department (ED) and approached for enrollment in the program. Patients who were eligible for admission but refused HaH admission, or those who were identified as eligible for admission but for whom HaH clinicians were not available were enrolled as control patients.

Intervention. The HaH intervention included physician or nurse practitioner visits at home to provide acute care services including physical examination, illness and vital signs monitoring, intravenous infusions, wound care, and education regarding the illness. Nurses visited patients once or more a day to provide most of the care, and a physician or nurse practitioner saw patients at least daily in person or via video call facilitated by the nurse. A social worker also visited each patient at least once. Medical equipment, phlebotomy, and home radiography were also provided at home as needed. Patients were discharged from acute care when their acute illness resolved; subsequently, nurses and social workers provided self-management support and coordination of care with primary care.

Main outcome measures. Main study outcome measures include duration of the acute care period (length of stay [LOS]) and 30-day all-cause hospital readmissions or ED visits, transfer to a skilled nursing facility, and referral to a certified home health care agency. LOS was defined as being from the date the patient was listed for admission by an ED physician to the date that post-acute care was initiated (for HaH) or hospital discharge (for control patients). Other measures include patient's rating of care measured using items in 6 of the 9 domains of the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey that were most salient to care

at home, including communication with nurses, communication with physicians, pain management, communication about medicines, discharge information, and overall hospital rating.

Main results. The HaH clinical team approached 460 patients and enrolled 295 to the program. A total of 212 patients who were admitted to the hospital were enrolled as control patients. HaH patients were older than control patients, with an average age of 76.9 years (SD, 16.6) and 71.5 years (SD 13.8), respectively, and more likely to have at least 1 functional limitation (71.5% vs. 55.5%). The most frequent admission diagnoses to HaH were UTIs, CAP, cellulitis, and CHF. HaH patients had a shorter hospitalization LOS (3.2 days) compared with the control group (5.5 days; 95% confidence interval [CI], –1.8 to –2.7 days). HaH patients were less likely to have 30-day all-cause hospital readmissions (8.6% vs. 15.6%; 95% CI, –12.9% to –1.1%) and 30-day ED revisits (5.8% vs. 11.7%) compared to controls. Analysis adjusted for age, sex, race, ethnicity, education, insurance type, physical function, general health, and admitting diagnosis found that HaH patients had lower odds of hospital readmission (odds ratio [OR], 0.43; 95% CI, 0.36-0.52) and lower odds of ED revisits (OR, 0.39; 95% CI, 0.31-0.49). HaH patients reported higher ratings for communication with nurses and physicians and communication about medicines when compared with controls; they were also more likely to report the highest rating for overall hospital care (68.8% vs. 45.3%). Scores for pain management were lower for HaH patients when compared with controls.

Conclusions. Patients receiving care through the HaH program were less likely to be readmitted at 30 days after hospital discharge, had lower hospital LOS and reported higher ratings of care when compared to patients receiving care in the hospital. The study demonstrated the potential benefits of the HaH model of care for adults who need inpatient hospitalization.

Commentary

This study adds to the literature on outcomes associated with HaH programs. The first study of the HaH model in the United States was published in 2005,[1] and despite the early demonstration of its feasibility and outcomes in this and subsequent studies,[2,3] HaH models have not been widely adopted, unlike in other countries with integrated health care systems.[4] One of the primary reasons this model has not been adopted is the lack of a specific payment mechanism in Medicare fee for service for HaH. Implementation of the HaH program described in the current study was an effort funded by a CMS innovation award to test the effect of models of care with the potential of developing payment mechanisms that would support further dissemination of these models. The results from the current study were encouraging and have led to the Physician-Focused Payment Model Technical Advisory Committee's unanimous recommendation to the U.S. Department of Health and Human Services for full implementation in 2017.

The current study does have certain limitations. It is not a randomized trial, and thus control group selection could be affected by selection bias. Also, the study was conducted in a single health system and thus may have limited generalizability. Nevertheless, this study was designed based on prior studies of HaH, including randomized and non-randomized studies, that have demonstrated benefits similar to the current study. The finding that HaH patients reported worse pain control than did patients hospitalized in the inpatient setting, where staff is available 24 hours a day, may suggest differences in care that is feasible at home versus in the inpatient setting. Finally, because it is a bundled program that includes both HaH and a post-discharge care transition program, it is unclear if the effects found in this evaluation can be attributed to specific components within the bundled program.

Applications for Clinical Practice

Patients, particularly older adults, may prefer to have hospital-level care delivered at home; clinicians may consider how HaH may allow patients to avoid potential hazards of hospitalization,[5] such as inpatient falls, delirium, and other iatrogenic events. The HaH program is feasible and safe, and is associated with improved outcomes of care for patients.

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References

1. Leff B, Burton L, Mader SL, et al. Hospital at home: feasibility and outcomes of a program to provide hospital-level care at home for acutely ill older patients. *Ann Intern Med*. 2005;143: 798-808.
2. Caplan GA, Sulaiman NS, Mangin DA, et al. A meta-analysis of "hospital at home". *Med J Aust*. 2012;197:512-519.
3. Mader SL, Medcraft MC, Joseph C, et al. Program at home: a Veteran Affairs healthcare program to deliver hospital care in the home. *J Am Geriatr Soc*. 2008;56: 2317-2322.
4. Montalto M. The 500-bed hospital that isn't there: the Victorian Department of Health Review of the hospital in the home program. *Med J Aust*. 2010;193:598-601.
5. Creditor MC. Hazards of hospitalization. *Ann Intern Med*. 1993;118:219-223.