A Systematic Review and Meta-analysis of Studies Comparing Readmission Rates and Mortality Rates in Patients With Heart Failure

Femida H. Gwadry-Sridhar, PhD(C); Virginia Flintoft, MSc; Douglas S. Lee, MD; Hui Lee, MD†; Gordon H. Guyatt, MD

Background: Heart failure is the leading cause of hospitalization and readmission in many hospitals worldwide. We performed a meta-analysis to evaluate the effectiveness of multidisciplinary heart failure management programs on hospital admission rates.

Methods: We identified studies through an electronic search and mortality using 8 distinct methods. Eligible studies met the following criteria: (1) randomized controlled clinical trials of adult inpatients hospitalized for heart failure enrolled either at the time of discharge or within 1 week after discharge; (2) heart failure-specific patient education intervention coupled with a postdischarge follow-up assessment; and (3) unplanned readmission reported. Four reviewers independently assessed each study for eligibility and quality, achieving a weighted $k$ of 0.73 for eligibility and 0.77 for quality. For each study we calculated the relative risk for readmissions and mortality for patients receiving enhanced education relative to patients receiving usual care.

Results: A total of 529 citation titles were identified, of which 8 randomized trials proved eligible. The pooled relative risk for hospital readmission rates using a random-effects model was 0.79 (95% confidence interval, 0.68-0.91; $P<.001$; heterogeneity $P=.25$). There was no apparent effect on mortality (relative risk, 0.98; 95% confidence interval, 0.72-1.34; $P=.90$; heterogeneity $P=.20$). Data were insufficient to meaningfully pool intervention effects on quality of life or compliance.

Conclusion: This systematic review suggests that specific heart failure–targeted interventions significantly decrease hospital readmissions but do not affect mortality rates.

Heart Failure (HF) is characterized by a high rate of hospital readmission and death, significant functional compromise, reduced quality of life (QOL), and increased caregiver burden.1 Data from the National Health and Nutrition Examination Survey I indicated that 71.8% of men and 59.5% of women aged 65 to 74 years died within 10 years of their self-reported onset of HF.2 These data are similar to the rates observed in Nova Scotia,3 the Framingham study,4 and the National Health and Nutrition Examination Survey.5

The increase in the prevalence of HF6-9 represents an enormous burden to our health care system when coupled with extended and frequent hospital stays. It is conceivable that multidisciplinary patient interventions could reduce the frequency of admissions and length of hospital stay, decreasing patient suffering and the demand on our health care system. Two other systematic reviews have been performed in this area.10,11 Their limitations included the inclusion of duplicate studies and inclusion of one study that incorporated patients with both congestive heart failure and chronic obstructive pulmonary disease.10 Other studies have primarily been qualitative reviews of published studies.

The present study addresses the following question: Do patients with HF participating in a peridischarge multidisciplinary patient treatment program have a reduced rate of readmission and mortality compared with patients who receive usual care?

METHODS

RESEARCH TEAM

A group of 4 health services researchers with an interest in HF participated in this systematic review. The team included a health services research nurse (V.F.) and pharmacist (F.H.G.-S.), a board-certified cardiologist (D.S.L.), and an internist from northern Ontario (H.L.). All of the participants had post-

Author Affiliations: Division of Critical Care, Department of Medicine, University of Western Ontario, and London Health Sciences Centre, London, Ontario (Dr Gwadry-Sridhar); Department of Health Policy, Management, and Evaluation, University of Toronto, Toronto, Ontario (Ms Flintoft); National Heart, Lung, and Blood Institute, Framingham, Mass (Dr D. S. Lee); and Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario (Drs Gwadry-Sridhar, H. Lee, and Guyatt).

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†Deceased.
graduate training in epidemiology. The senior author (G.H.G.) provided guidance on the choice of methods and meta-analytical tools to use in this review.

**LITERATURE SEARCH**

We used 5 strategies to identify studies: electronic databases, our own files, consultations with experts from North America and Europe, hand search of references in articles that met our criteria, and PubMed search using the related-articles feature for all studies meeting our eligibility criteria.

Electronic database searches were conducted on MEDLINE, HealthSTAR, and EMBASE. The MEDLINE search was performed on all files between 1966 and 2000 as follows: [“heart failure, congestive”/] and [adult/] and [patient readmission/s] or [exp disease management/] or [exp patient care team/cl, mt, og, ed, st, sn, td, ma, ut (classification, methods, organization & administration, education, standards, statistics & numerical data, trends, manpower, utilization)] or [exp follow-up studies/] or [“patient readmission/”] or [exp patient discharge] or [exp patient education/] or [exp aftercare/] or [patient care planning/] or [exp home care services, hospital-based/]. The HealthSTAR search was performed on all files between 1975 and October 2000. We also searched PubMed and the Cochrane Review. We hand-searched relevant journals including the *Journal of General Internal Medicine* and the *Archives of Internal Medicine*. We also hand-searched abstracts from relevant cardiology meetings. Two members of the research team (V.F. and F.H.G.-S.) reviewed citations, removed duplicates, and obtained the full text of all potentially relevant articles.

Our strategies yielded 529 unique citations: 199 from MEDLINE, 148 from HealthSTAR, 162 from EMBASE, and 20 from personal files, reference lists, and communication with experts (Figure 1). Of these, 94 were deemed potentially eligible for pretest selection. Two research trials in progress were identified and interim data were obtained from the principal investigators. A weighted $\kappa$ statistic was computed for agreement on study inclusion.

**QUALITY ASSESSMENT**

To assess the quality of the trials, we used the Jadad 5-point scale, modified slightly for our purpose. To obtain a perfect Jadad score, we required that the study be randomized with the method of randomization clearly described, patients and physicians be blinded, and the method of blinding that was deemed appropriate and withdrawals and dropouts be described. A total quality score was tested for agreement by means of a $\kappa$ weighted with quadratic weights for multiple raters. Studies achieving a score of 4.0 or more were designated high quality.

**SOURCES OF HETEROGENEITY: A PRIORI HYPOTHESES**

Differences in study outcomes may prove to be more than would be expected on the basis of chance alone, resulting in $P \leq 0.10$ for the test of heterogeneity. In participation of potentially statistically significant heterogeneity, we established 2 hypotheses in advance of performing our analyses, which may help explain differences in outcomes. The hypotheses were as follows: differences in the length of follow-up may account for differences in outcomes; and differences in the methodology of the intervention, eg, telephone follow-up vs home visit vs HF clinic visit, may account for variability resulting in differences in outcomes.

**STUDY SELECTION**

The research team developed and agreed to the selection criteria used for study inclusion in advance. All research studies were required to be randomized controlled trials involving patients older than 18 years. Specific inclusion criteria were as follows:

1. The target population: patients who were hospitalized for HF and enrolled in the trial either during hospitalization or immediately before or after discharge. Both an intervention and a control group were required.

2. The intervention: a patient education intervention directed at increasing patients’ knowledge of their HF diagnosis, signs, symptoms, and/or treatment. The professional designation of the intervention team was not critical provided it was multidisciplinary. Patients not randomized to the intervention group received usual care delivered by a family physician, internist, or cardiologist.

3. Primary outcome: unplanned readmission for HF for all causes in the follow-up period for a minimum of 3 months after discharge. Other outcomes of interest included mortality, compliance, and QOL. Studies were included provided they had collected data relevant to the primary outcome regardless of the measure of readmission.

These criteria were applied to all potentially relevant titles and abstracts. The initial assessment was performed by 2 of the team members (V.F. and F.H.G.-S.). Articles found eligible by either reviewer on the initial round were retrieved. Each of the 4 individuals (F.H.G.-S., V.F., H.L., and D.S.L.) independently evaluated retrieved articles to determine eligibility. Each reviewer was asked to rate each as “include” or “exclude.” If the retrieved article passed full eligibility criteria, it was independently reviewed in detail by all 4 reviewers. All reviewers participated in resolving disagreements. Disagreements in the first phase were resolved by including the article in the second phase of the review.
Disagreements in the review of the full article were settled through conference until a consensus was reached.

Eight published articles and a study in progress were included in the overview.13-21 Subsequently, 1 study was excluded because it represented publication of the same patient cohort but extended follow-up periods of 6 months and 18 months.21 We opted to keep the article with 6 months of follow-up, as it fell within the follow-up period reported by other trials.14 We were left with 8 randomized controlled trials for meta-analysis. The primary author (F.H.G.-S.) in consultation with the authors (D.S.L.) used the meta-analysis program RevMan.25 The reviewers did the analyses independently as a quality assurance measure. There was total agreement between the 2 analyses.

Our attempt to compute the difference in QOL scores between the intervention and usual care groups at different points during the follow-up period was abandoned because of a lack of consistency in QOL measurement tools. However, trends in QOL were noted.

### RESULTS

We identified 8 publications13-20 that met our eligibility criteria. The weighted $kappa$ agreement statistic for study inclusion was 0.73 (SE, 0.09). The $kappa$ statistic for quality assessment weighted with quadratic weights for multiple reviewers was 0.77 (SE, 0.07). A summary of the studies selected and the outcomes they collected is shown in Table 1.

All but 2 studies randomized patients equally to intervention and usual care groups.14,15 One study intentionally used a 2:1 randomization scheme.16 The primary author of that study (C. Cline, Malmo University Hospital, Malmo, Sweden; personal communication; February 28, 2003) indicated that randomization was performed according to a design proposed by Zelen.26 In this study, the patients were randomized first, and active and control patients were given different patient information according to group. A greater number of patients in the intervention group with- held consent.16 Mean (SD) age ranged from 71.0 to 80.3 years (6.8 years) across the studies. The proportion of males in all studies ranged between 0.37 and 0.62. Only one of the studies16 reported on the distribution of New York Heart Association class, and it excluded patients with class IV HF.

Five of the studies required at least 1 home visit within 1 to 2 weeks of discharge from the hospital (Table 2).13-16,20 Three studies operated an HF clinic.14,15 Nurses who collaborated with physicians on an “as required” basis managed all clinics. Patients were required to attend at least 1 appointment in 2 studies and attendance was voluntary in the third.16 If a patient chose not to attend the clinic, the nurse telephoned once per month for the duration of follow-up. In one of the studies, the research nurse acted as a liaison with a community health nurse who visited the home as necessary.18 The Serxner et al study19 differed from the others because the intervention was conducted by mail and follow-up was conducted by a telephone survey performed by non-medical personnel. This study scored consistently lower than others for methodologic quality.

### Table 1. Summary of Study Characteristics

<table>
<thead>
<tr>
<th>Source</th>
<th>Country</th>
<th>Sample size</th>
<th>Total</th>
<th>Intervention</th>
<th>Control</th>
<th>Age, mean ± SD, y</th>
<th>Sex, % M</th>
<th>NYHA class</th>
<th>Follow-up, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cline et al, 1998</td>
<td>Sweden</td>
<td>110</td>
<td>75 ± 5.1</td>
<td>73 ± 9</td>
<td>76 ± 11</td>
<td>77.3 ± 6.1</td>
<td>48</td>
<td>III-IV</td>
<td>12</td>
</tr>
<tr>
<td>Jaarsma et al, 1998</td>
<td>The Netherlands</td>
<td>80</td>
<td>76 ± 11</td>
<td>74 ± 10</td>
<td>78.0 ± 6.3</td>
<td>78.9 ± 9.3</td>
<td>41</td>
<td>II-IV</td>
<td>9</td>
</tr>
<tr>
<td>Stewart et al, 1995</td>
<td>Australia</td>
<td>49</td>
<td>80.0 ± 6.3</td>
<td>77.0 ± 5.3</td>
<td>80.3 ± 6.8</td>
<td>78.4 ± 6.1</td>
<td>50</td>
<td>III-IV</td>
<td>6</td>
</tr>
<tr>
<td>Serxner et al, 1998</td>
<td>United States</td>
<td>55</td>
<td>80.1 ± 5.9</td>
<td>78.8 ± 5.6</td>
<td>80.1 ± 5.9</td>
<td>64.8 ± 11.7</td>
<td>37</td>
<td>NR</td>
<td>18</td>
</tr>
<tr>
<td>Rich et al, 1999</td>
<td>United States</td>
<td>53</td>
<td>66.8 ± 14.3</td>
<td>64.8 ± 11.7</td>
<td>66.8 ± 14.3</td>
<td>64.8 ± 11.7</td>
<td>51</td>
<td>III (62%)</td>
<td>12</td>
</tr>
<tr>
<td>Ekman et al, 2001</td>
<td>Sweden</td>
<td>55</td>
<td>NR</td>
<td>48</td>
<td>41</td>
<td>37</td>
<td>12</td>
<td>III-IV</td>
<td>12</td>
</tr>
<tr>
<td>Gwadry-Sridhar et al, 2001</td>
<td>Canada</td>
<td>48</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>3</td>
<td>12</td>
<td>III-IV</td>
<td>12</td>
</tr>
</tbody>
</table>

Characteristics:
- Country
- Sample size
- Total
- Intervention
- Control
- Age, mean ± SD, y
- Sex, % M
- NYHA class
- Follow-up, mo

Abbreviations: C, control (usual care); CPL, compliance; ED, emergency department visits; EFS, event-free survival; HCC, number of health care contacts; HF, heart failure; M, mortality; NR, not reported; NYHA, New York Heart Association; PR, proportion of unplanned readmission; PS, patient satisfaction; QOL, quality of life; R/D, frequency of unplanned readmission plus death; RR, rate of readmission; T1st, time to first end point; TDH, total days of hospitalization.

*Rich et al initially studied patients for 3 months, then followed up these patients for an additional 9 months.*
Table 2. Description of Study Interventions

<table>
<thead>
<tr>
<th>Source</th>
<th>Before Discharge</th>
<th>Intervention</th>
<th>After Discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rich et al,14 1993</td>
<td>Visits, 1/d: RN, dietitian, or geriatric cardiologist; educ: symptoms, medications, treatment, follow-up, 1.5-2.0-g sodium diet, weight (scale provided), medication regimen simplified</td>
<td>24-48 h: home visit; hospital’s home-care RN; repeat educ and cardiac physical examination; week 1: home visit × 3; study RN telephone assessment</td>
<td></td>
</tr>
<tr>
<td>Rich et al,15 1995</td>
<td>Visits, 1/d: RN, dietitian, or geriatric cardiologist; education: symptoms, medications, treatment, follow-up, 1.5- to 2.0-g sodium diet, weight (scale provided), medication regimen simplified</td>
<td>24-48 h: home visit; hospital’s home-care RN; repeat educ and cardiac physical examination; week 1: home visit × 3; study RN telephone assessment</td>
<td></td>
</tr>
<tr>
<td>Serxner et al,19 1998</td>
<td>NA</td>
<td>Educational information mailed every 3-4 wk</td>
<td></td>
</tr>
<tr>
<td>Ekman et al,18 1998</td>
<td>RN visit, educ, patients and family; meds; compliance; symptoms</td>
<td>7 d: RN telephones to invite patient to RN-run OP clinic; drop in or telephone as needed; if no visit, RN telephones monthly; direct admission from clinic to CHF floor; RN works with primary MD and home health RN</td>
<td></td>
</tr>
<tr>
<td>Cline et al,16 1998</td>
<td>Oral/video session; patients and family; pathophysiology, medications, and non-medical treatment; compliance; self-management diuretics; symptoms; weight, ankle circulations</td>
<td>14 d: 1-h session by RN directed OP clinic; drop in or telephone as needed; interview with RN at 8 mo</td>
<td></td>
</tr>
<tr>
<td>Stewart et al,13 1998</td>
<td>NA</td>
<td>1-2 wk: home visit from cardiology RN; repeat if ≥2 readmissions/6 mo; 3 and 6 mo: telephone</td>
<td></td>
</tr>
<tr>
<td>Jaarsma et al,20 1999</td>
<td>RN assess, CHF educ (patient/family): symptoms; sodium/fluid restriction; compliance; psychosocial/sociological impact + discharge plan</td>
<td>7 d: RN telephone; 10 d: home visit; 1, 3, and 9 mo: interview</td>
<td></td>
</tr>
<tr>
<td>Gwadry-Sridhar et al,17 2001</td>
<td>Booklets, one-on-one teaching by RN and research pharmacist; memory aids, counseling; research in progress</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; educ, education; MD, physician; NA, not available; OP, outpatient; RN, registered nurse.

Length of follow-up varied across the trials. One followed up patients for 3 months,19 another had 3 months of active intervention followed by 9 months of observation,13 and 3 studies followed up their patients for 6 months13,18,19; one of these continued observation and data collection for an additional 9 months.13 The follow-up periods were 9 months16 and 12 months16,17 for the remaining 3 studies. All studies measured proportion or rate of readmission as a primary or secondary outcome. Mortality was measured in 6 of 8 studies, and health-related quality of life (HRQOL) was measured in 3 of 8 studies.

Results were plotted on a single graph to provide a visual representation of interstudy consistency in outcome (Figure 2 and Figure 3). The individual study and pooled risk ratios for readmission using a random-effects model are plotted in Figure 2. Individual study RRs ranged from 0.55 (95% CI, 0.33-0.91) for the Serxner study19 to 1.07 (95% CI, 0.82-1.38) for the Ekman et al study.18 The range of readmissions in the control group was 39.1% to 64.5%, and in the intervention group, 27% to 61%. The pooled RR for readmission at 0.79 was significant (P < .001). The Cochran Q χ² test for heterogeneity, at P = .25, suggested that study variability was within acceptable levels. The relative risk reduction was 21% in favor of the intervention group. The absolute risk reduction was 11% with a number needed to treat of 9.

The individual and pooled RRs for mortality using a random-effects model are plotted in Figure 3 for 6 of the 8 studies that collected mortality data. Individual study RR ranged from 0.49 (95% CI, 0.20-1.20) to 1.56 (95% CI, 0.88-2.76). The pooled RR was 0.98 (95% CI, 0.72-1.34), which was not significant (P = .90). The Cochran Q χ² statistic for heterogeneity was 7.23 (P = .20).

To assess the potential for publication bias, we used a funnel plot (Figure 4). The RR for readmission in each study is plotted against the weight of the study, represented by the sample size.23 The funnel plot showed no suggestion of publication bias.

We could not satisfy our intention to analyze the difference in QOL between the intervention and usual-care groups as a secondary outcome. Health-related QOL was measured in 4 of 8 studies. Three of these studies used different disease-specific instruments, for which validity and responsiveness have been published.26 Two of the 3 studies favored intervention by showing a significant improvement in HRQOL at the end of their respective follow-up periods from baseline.15,16 In one study,17 there was no difference between the 2 groups at baseline or at 1 year, although both groups improved from baseline. On the basis of the limited data available,...
able on HRQOL, we did not pool the data. We believed that, because of the different time frames used for data collection and the limited amount of data available on the specific domains of the 36-Item Short-Form Health Survey, pooling would add little to our understanding of the impact of these interventions on HRQOL.

COMMENT

In this meta-analysis, we performed a comprehensive literature search, specified inclusion and exclusion criteria, and conducted rigorous data analysis. We made a substantive effort to contact the primary authors of trials that required an explanation about the design or results. To calculate the summary estimates of treatment, we used a random-effects model that provides a conservative effect of the treatment effects by incorporating both between-study and within-study variation. The strength of this meta-analysis can be assessed only through the strength of the individual studies. The main limitation is that all of these studies have small sample sizes that leave the review more open to publication bias.

Notwithstanding this limitation, patients with HF who have the opportunity to participate in a peri-discharge program seem to benefit from a reduced risk of readmission. This fact in itself has significant implications for patients and their families, as the morbidity incurred by the patients is significant and impacts HRQOL. Future studies should be larger and have longer follow-up periods, ideally 3 to 5 years.

Our search identified 8 randomized controlled studies that compared a nonpharmacologic patient education intervention directed at increasing patient knowledge of HF compared with usual care. All of these studies had a score of 4 or more, meeting our quality assessment criteria. Concealment was definitive and acceptable in 6 (75%) of the studies, questionable in 1 study, and absent in 1 study. Blinding to the outcomes of readmission or death was not evident in most of the studies. We do not consider this to be a limitation, as the lack of blinding to these outcomes is not subject to bias.

Our pooled analyses for readmissions demonstrated that an educational intervention in patients with HF as part of a program resulted in statistically significant relative risk reduction in readmissions. Seven of the 8 studies we pooled favored intervention, while 1 favored control. The number needed to treat to prevent 1 readmission was 9. The pooled data on mortality favored neither intervention nor control. The
data on secondary outcomes such as HRQOL were inconclusive; however, 2 of the 3 studies showed through disease-specific measures that HRQOL improved significantly in patients receiving an intervention.\textsuperscript{15,16} We are aware of one other meta-analysis in this area, with results similar to ours.\textsuperscript{10}

We did not include a cost-effectiveness analysis as part of this meta-analyses because of the lack of data from the studies we used. However, the results of this review illustrate that there is a realizable potential to impact on readmissions, which are very costly to both the health care system and the patient. Even a small reduction in the number of readmissions can affect resource use. With realized savings in hand, directing these resources toward validated patient education endeavors could be considered.

Where does this leave us in terms of how we intervene with patients who have HF? Our findings support the implementation of an HF program that includes a discharge program aimed at improving medication compliance and lifestyle adjustments. These types of interventions provide us with a tangible way to reduce the rate of readmission by 21\%, providing an absolute reduction of 4 patients as a minimum, up to 14 patients. The potential of implementing an noninvasive intervention that can reduce hospital visits helps patients and potentially conserves resources.

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Correspondence: Femida H. Gwadry-Sridhar, PhD(C), Division of Critical Care, Department of Medicine, London Health Sciences Centre, Victoria Campus, 375 South St, London, Ontario, Canada N6A 4G5 (Femida.GwadrySridhar@lhsc.on.ca).

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REFERENCES


