Early integration of palliative care versus standard cardiac care for patients with heart failure (EPCHF): a multicentre, parallel, two-arm, open-label, randomised controlled trial

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Summary

Background Heart failure is a substantial global health concern that severely affects patients' quality of life. We aimed to compare the effects of early integration of palliative care (EIPC) and standard cardiac care on health status and mood of patients with non-terminal heart failure.

Methods EPCHF was a multicentre, parallel, two-arm, open-label, randomised controlled trial carried out at University Hospital Bonn and University Hospital Düsseldorf in Germany. Eligible patients (aged 18 years or older) had heart failure, with New York Heart Association class II or more and NT-proBNP concentrations greater than or equal to 400 pg/mL. Patients were randomly assigned (1:1) to receive EIPC with standard cardiac care or standard cardiac care alone. Randomisation was computer-generated with allocation concealment, variable block sizes, and stratification by investigational site. The primary endpoints were health status and mood, measured every 3 months over 12 months using the Functional Assessment of Chronic Illness Therapy–Palliative Care (FACIT–PAL) and the Kansas City Cardiomyopathy Questionnaire (KCCQ), analysed by intention to treat. This trial is registered with DRKS.de, DRKS00013922.

Findings Between May 21, 2019, and Nov 15, 2021, 843 patients were assessed for eligibility, 205 of whom were enrolled (100 assigned to EIPC and 105 assigned to standard cardiac care). 143 (70%) patients were male and 62 (30%) were female. Over 12 months, both groups significantly improved in FACIT–PAL and KCCQ Overall Summary Score (OSS) with no significant differences between the groups (FACIT–PAL adjusted mean difference 0·98 points [95% CI –1·28 to 3·23]; p=0·40; KCCQ-OSS adjusted mean difference –2·06 points [–7·89 to 3·78]; p=0·49). Nine (9%) patients in the EIPC group and seven (7%) patients in the standard cardiac care group died from any cause, with no significant differences in time to death between the two groups (hazard ratio [HR] 1·32 [95% CI 0·49 to 3·54]; p=0·58). 22 (22%) patients in the EIPC group and 21 (21%) patients in the standard cardiac care group were hospitalised at least once due to heart failure, with no significant differences in time to heart-failure-related hospitalisation between the two groups (HR 1·09 [0·61 to 1·98]; p=0·77). 70 (70%) patients in the EIPC group and 62 (59%) in the standard cardiac care group had any adverse events (p=0·10).

Interpretation In this open-label, randomised clinical trial, standard cardiac care, featuring guideline-directed optimisation of medical therapy and regular 3-monthly follow-ups was found to be as effective as when combined with EIPC in improving health status and mood in patients with non-terminal heart failure. Future clinical practices should consider EIPC based on individual patient needs.

Funding Federal Ministry of Education and Research.

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Introduction

Heart failure is a major and escalating global health concern, affecting millions of individuals worldwide.[1] Despite advancements in medical therapies, a large proportion of patients with heart failure continue to struggle with burdensome symptoms that substantially impair their quality of life, similar to symptoms in patients with cancer.[2–5] In response, the application of palliative care, traditionally associated with managing terminal malignant diseases, is now being explored as a promising complementary strategy for those with heart failure.[6,7]

Palliative care provides a comprehensive, multidisciplinary approach that addresses not only the physical symptoms but also the psychosocial, emotional, and spiritual dimensions of patient care.[8] Because symptoms are prevalent even in non-terminal stages of heart failure, palliative care is expanding its scope to encompass patients at earlier stages of their illness.[9] This early integration of palliative care (EIPC)

Lancet Healthy Longev 2024

Published Online
https://doi.org/10.1016/j.lanhl.2024.08.006

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Research in context

Evidence before this study

On April 7, 2024, we searched PubMed for studies investigating the benefits of early integration of palliative care (EIPC) in patients with symptomatic, non-terminal heart failure, published in English from database inception to May 22, 2019, the time of trial initiation. We used the search terms "heart failure" AND "early" AND "palliative care". Animal studies were excluded. Of 171 results, we identified nine clinical trials, among which only two (ENABLE CHF-PC and CASA trials) were relevant randomised controlled trials. Both trials did not demonstrate improved health status with EIPC, despite showing improvements in some secondary outcomes such as pain intensity and interference in the ENABLE CHF-PC trial, and depression and fatigue in the CASA trial. The ENABLE CHF-PC trial included a majority African American population and was conducted over a relatively short duration of 16 weeks.

Added value of this study

This study was designed to evaluate the effect of integrating EIPC with guideline-directed standard cardiac care on health status and mood of patients with non-terminal heart failure. EIPC was delivered by a multidisciplinary palliative care team following the palliative care standards set by the National Consensus Project for Quality Palliative Care. Over a 12-month period, both EIPC and standard cardiac care groups showed significant improvements in health status and mood, with no significant differences between the groups, apart from for the secondary outcome of spiritual wellbeing, which was significantly improved for those in the EIPC intervention, although with no significant differences between groups at 12 months.

Implications of all the available evidence

The findings underscore the potential to optimise management of patients with heart failure who are not in terminal stages of their illness. The integration of EIPC appears to enhance spiritual wellbeing, as shown in our study, and to alleviate pain and reduce interference with daily activities, as shown in the ENABLE CHF-PC study. These results highlight the necessity to refine intervention strategies and adopt a more personalised approach that considers disease severity and patient preferences. Such measures could lead to more targeted and efficient use of health-care resources and improve patient outcomes.

holds potential to alleviate symptoms, enhance health-related quality of life, and ultimately improve overall patient outcomes.

To investigate this hypothesis among patients with heart failure, we aimed to assess the effect of EIPC on health status and mood in patients with heart failure, compared with standard cardiac care.

Methods

Study design

EPCHF was a multicentre, parallel, two-arm, open-label, randomised controlled trial carried out at University Hospital Bonn and University Hospital Düsseldorf in Germany. The study protocol and data safety monitoring plan were approved by the University of Bonn Ethics Commission (study code: MED2-201604_EPCHF). This trial is registered with DRKS.de, DRKS00013922.

Participants

Eligible patients (aged 18 years or older) had heart failure with reduced ejection fraction or heart failure with preserved ejection fraction with natriuretic peptide B concentrations greater than or equal to 100 pg/mL or NT-proBNP concentrations greater than or equal to 400 pg/mL; had a New York Heart Association functional class of II or more; and had the ability to comply with study instructions and complete all required visits. Several exclusion criteria were also in place, including inability to read, understand, or respond to questions in the German language, being in the intensive care unit and requiring mechanical ventilation, awaiting a heart transplantation or having received a heart transplant, having a non-cardiac terminal illness, simultaneous participation in another study, or being pregnant, planning for pregnancy, or currently breastfeeding.

Written informed consent was obtained from all patients, following the principles of the Declaration of Helsinki of the World Medical Association. Gender data were collected via self-report, allowing participants to identify their gender as they see fit without predefined categories. Race and ethnicity data were not collected in this study. A comprehensive publication detailing the rationale and design of the EPCHF trial is available for reference.[10]

Randomisation and masking

Eligible patients were randomly assigned (1:1) to receive standard cardiac care or EIPC in addition to standard cardiac care. Randomisation was done using a computerised block randomisation program with variable block sizes, stratified by the investigational site. Allocation concealment was ensured through computer-generated randomisation, performed using a secure REDCap database (Research Electronic Data Capture, Vanderbilt University, Nashville, TN, USA) prepared before the start of the trial. Due to the collaborative and multidisciplinary nature of the intervention, blinding was not feasible. Consequently, patients were aware of their treatment allocation throughout the study. Randomisation was managed by the Institut für Medizinische Biometrie, Informatik und Epidemiologie at University Hospital Bonn.

Procedures

The first group of patients received standard cardiac care as per established guidelines.[1,11] Additionally, they underwent regular outpatient follow-ups every 3 months for a period of

1 year. The primary objective of these follow-ups was to assess the medical condition of the patients and to refine therapeutic strategies. If further help or reassurance with medication was needed, patients or their treating doctors could request additional support from dedicated heart failure nurses, regardless of the patient's randomly assigned group. These nurses provided supplementary telephone support, starting with calls every 2 weeks that were gradually reduced to monthly and then as needed, based on the severity of the patient's condition and their ability to manage independently. During these calls, nurses delivered education about the condition and ensured adherence to medical regimens.

The second patient group received monthly EIPC consultations in addition to the cardiac care provided to the standard cardiac care group. The integration of palliative care into cardiac care aimed to specifically address patients' psychosocial and spiritual concerns in collaboration with the cardiology team. The multidisciplinary palliative care team included board-certified physicians and qualified social workers from the German Association for Palliative Medicine, all with extensive experience in palliative care. The palliative care team provided care exclusively to patients in the EIPC group. None of its members interacted with patients in the standard cardiac care group, ensuring a clear distinction in care provision between the two study groups

Patients in the EIPC group were scheduled for monthly consultation visits, typically lasting 30–60 min, at the outpatient clinics of the respective hospitals. The intervention was personalised and adapted to the individual needs and preferences of the patients, ensuring that consultation times with the social worker were adjusted as necessary. These consultations adhered to the outpatient palliative care guidelines established by the National Consensus Project for Quality Palliative Care.[12] Detailed information about EIPC is provided in the appendix (p 1). Data were collected using the online platform REDCap.

A data and safety monitoring board was set up to supervise the trial's progress and outcomes at two predetermined enrolment milestones: when 33% and 66% of the participants were enrolled. The main role of the data and safety monitoring board was to evaluate safety data from both trial groups. It had the authority to terminate the study in cases of evident harm to participants, but not solely based on evidence indicating a lack of efficacy.

Outcomes

The primary objective was to compare the effects of standard cardiac care and EIPC on the health status and mood of patients with heart failure over a 12-month period. This comparison was assessed using two standardised questionnaires at 3-month intervals: the Functional Assessment of Chronic Illness–Therapy Palliative Care (FACIT–PAL) and the Kansas City Cardiomyopathy Questionnaire (KCCQ).

The FACIT–PAL is a widely used questionnaire that evaluates the effect of palliative care interventions on the wellbeing of individuals with chronic illnesses. It consists of 14 questions covering multiple domains associated with physical, emotional, social, and functional wellbeing. These questions are scored collectively on a single scale, with higher values indicating a higher level of health status.[13] A change of 12·5 points is considered a minimal clinically important difference.[14]

The KCCQ is specifically designed to evaluate health status in individuals with heart failure. It consists of 23 questions categorised into five domains: physical limitations, social limitations, symptoms, self-efficacy, and quality of life. Each question is scored on a scale of 0 to 100, with higher scores indicating a lower burden of symptoms and better overall health status. With the exception of self-efficacy, all domains of the KCCQ can be further condensed into a single comprehensive summary score known as the KCCQ Overall Summary Score (KCCQ-OSS).[15] A change of 5 points on the KCCQ-OSS is considered a minimal clinically important difference.[16]

Secondary endpoints included a comprehensive set of measures aimed at further evaluating the effects of both standard cardiac care and EIPC interventions on various aspects of patients' wellbeing and clinical outcomes. These endpoints were evaluated using the Hospital Anxiety and Depression Scale (HADS), the minimal documentation system (MIDOS) for palliative medicine, and the Functional Assessment of Chronic Illness Therapy–Spiritual Well-Being 12 (FACIT–SP12). The HADS was conducted every 3 months, whereas the MIDOS and FACIT–SP12 were conducted at baseline and at the final follow-up visit at 12 months. Time to all-cause mortality and heart-failure-related hospitalisation were also compared between the two groups.

HADS is a commonly used questionnaire aimed at assessing anxiety and depression levels. It features 14 items divided into two subscales: one for anxiety and the other for depression.[17] The minimal clinically important difference for HADS is 1·7 points.[18] MIDOS, the updated German adaptation of the Edmonton Symptom Assessment Scale, includes a 13-question survey. 12 of these questions evaluate physical and emotional distress, with patients rating the intensity of their symptoms on a 4-point Likert scale, on which higher scores signify greater severity. There is also a question dedicated to wellbeing, for which higher values indicate better overall wellbeing.[19] The minimal clinically important difference for MIDOS is 1 point. FACIT–SP12 is a 12-item questionnaire designed to evaluate spiritual wellbeing. It uses a 5-point Likert scale, with higher values indicating a higher degree of wellbeing.[20] These questionnaires were chosen due to their reliability in previous studies addressing palliative care in patients with heart failure.[21]

See Online for appendix

Additionally, adverse events were systematically monitored and recorded for both the EIPC and standard cardiac care groups throughout the trial to ensure participant safety.

Statistical analysis

As per Rogers and colleagues,[14] the FACIT–PAL questionnaire's standard deviation was around 30 points.

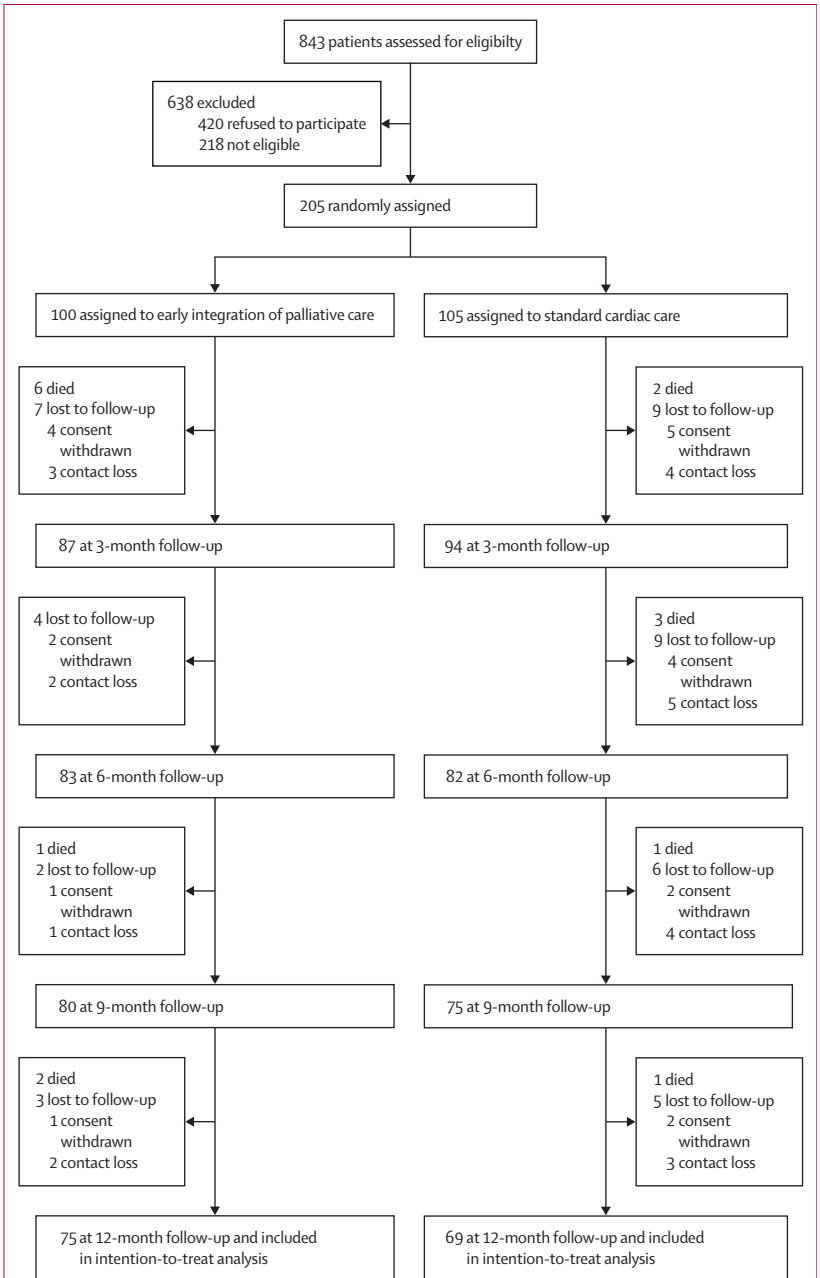

Figure 1: **Trial profile**

With 80 patients per group, an 80% powered *t* test could detect 13·5 point differences. Considering a 20% dropout rate, 200 patients (100 per group) were required. Similarly, using a standard deviation of 22·5 points for the KCCQ questionnaire, 80 patients per group would achieve 80% power to detect 10 point differences. These assumptions provided estimated sample sizes for detecting significant group differences.[14]

Categorical variables are presented as counts (percentages), and continuous variables are reported as mean (SD) for variables with normal distribution or median (IQR) for variables with non-normal distribution. The normal distribution was assessed using Shapiro-Wilk tests. To compare the differences between the two independent groups, the Mann–Whitney *U* test was used for non-normally distributed data, while the independent *t* test was used for normally distributed data. The within-group analysis for non-normally distributed data involved the Wilcoxon matched-pair signed-rank test, while the analysis for normally distributed data used the dependent *t* test.

The two primary endpoints were tested using a two-step procedure. First, the hypothesis of equal FACIT–PAL scores between the two treatment groups was tested with a two-sided *t* test at a 5% significance level. If this null hypothesis was rejected, the second hypothesis of equal KCCQ scores would be tested similarly. This procedure controlled the family-wise error rate at 5%.

The comparison of health status and mood scores between the two groups over the observational period was conducted using linear mixed-effects models, adjusted for corresponding baseline values and investigational site. All analyses (for both primary and secondary endpoints) were carried out following an intention-to-treat approach. According to the study protocol, missing data were generally not imputed. However, for the purpose of sensitivity analysis, a last observation carried forward imputation was performed for primary endpoints. To assess the robustness of our findings, we conducted an additional per-protocol analysis for the primary endpoints. The per-protocol population included patients who adhered fully to study protocol.

For time-to-event analyses, p values derived from a log-rank test were used for between-group comparisons. Hazard ratios (HRs) and associated 95% CIs for the treatment effects were estimated with the use of a Cox regression model. Additionally, time to first all-cause hospitalisation was analysed as a post-hoc outcome. A two-tailed p value less than or equal to 0·05 was considered statistically significant. Statistical analysis was done using SAS version 9.4.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between May 21, 2019, and Nov 15, 2021, 843 patients were assessed for eligibility, 205 of whom were enrolled in the study (100 in the EIPC group and 105 in the standard cardiac care group; figure 1). Enrolment included patients from both inpatient and outpatient settings. 143 (70%) patients were male and 62 (30%) were female. Median age was 67 years (IQR 56–78). Baseline health status and mood symptoms were similar between the two groups (table). 45 (22%) patients were lost to follow-up due to contact loss or withdrawal of consent (16 [16%] patients in the EIPC group and 29 [28%] in the standard cardiac care group). Detailed information on protocol deviations is in the appendix (p 2).

During the 12-month follow-up period, both groups showed significant improvements in FACIT–PAL scores from baseline to 12 months. The adjusted mean FACIT–PAL total score in the EIPC group increased by 4·85 points (95% CI 3·07 to 6·62; p<0·0001), and in the standard cardiac care group, it increased by 3·81 points (2·01 to 5·61; p<0·0001). However, these improvements were similar between the two groups at 12 months, with no statistically significant differences observed (adjusted mean difference 0·98 points [95% CI –1·28 to 3·23]; p=0·40; figure 2 and appendix pp 3–5). In the sensitivity analysis with last observation carried forward, the adjusted mean difference was 1·14 points (–0·76 to 3·03; p=0·24).

Similarly, both groups showed significant improvements in the KCCQ-OSS over the same follow-up period. In the EIPC group, the adjusted mean KCCQ-OSS improved by 22·58 points (95% CI 18·30 to 26·86; p<0·0001), and in the standard cardiac care group, it increased by 22·47 points (18·14 to 26·79; p<0·0001). These improvements were also similar between the two groups at 12 months, with no statistically significant differences found (adjusted mean difference –2·06 points [95% CI –7·89 to 3·78]; p=0·49; figure 3 and appendix pp 3–5). In the sensitivity analysis with last observation carried forward, the adjusted mean difference was –0·21 points (95% CI –5·92 to 4·76; p=0·83).

In the per-protocol population, both the FACIT–PAL and KCCQ-OSS scores were similar to the intention-to-treat analysis, with no significant difference between the EIPC and standard cardiac care groups at 12 months. For FACIT–PAL, the adjusted mean difference was 0·64 points (95% CI –1·90 to 3·17; p=0·62). For KCCQ-OSS, the adjusted mean difference was –1·93 points (–8·45 to 4·59; p=0·56; appendix p 6).

Both groups showed significant reductions in mean HADS anxiety scores and HADS depression scores over the 12 months (appendix p 5). However, no statistically significant differences were found between the groups at 12 months for anxiety or depression scores (appendix pp 5, 9–10).

At 12 months, both the EIPC and standard cardiac care groups showed significant reductions in MIDOS symptom intensity scores and significant increases in MIDOS wellbeing scores (appendix p 5). However, these positive changes were similar between the groups, with no significant differences observed in either MIDOS symptom intensity scores or wellbeing ratings (appendix pp 5, 11–12).

Significant improvement in the FACIT-SP12 spiritual wellbeing score was noted in the EIPC group at 12 months, but not in the standard cardiac care group (appendix p 5). However, the comparison between the two groups at 12 months showed no statistically significant difference (appendix pp 5, 13).

Over the 12-month follow-up period, 16 (8%) patients died from any cause (appendix p 8), with a median time from random assignment to death of 84 days (IQR 30–248). Nine (9%) patients in the EIPC group and seven (7%) patients in the standard cardiac care group died from any cause, with no significant differences in time to death between the two groups (HR 1·32 [95% CI 0·49–3·54]; p=0·58; appendix p 14).

Regarding the post-hoc analysis of all-cause hospitalisation, 51 (51%) patients in the EIPC group and 46 (44%) patients in the standard cardiac care group had at least one hospitalisation for any reason, with no statistically significant differences in time to hospitalisation between the two groups (HR 1·28 [95% CI 0·86–1·90]; p=0·23). 22 (22%) patients in the EIPC group and 21 (21%) patients in the standard cardiac care group were hospitalised at least once due to heart failure, with no significant differences in time to heart-failure-related hospitalisation between the two groups (HR 1·09 [0·61–1·98]; p=0·77; appendix p 7).

	All patients (n=205)	Early integration of palliative care group (n=100)	Standard cardiac care group (n=105)
Age, years	67 (56–78)	68 (57–78)	66 (55–77)
Sex			
Male	143 (70%)	75 (75%)	68 (65%)
Female	62 (30%)	25 (25%)	37 (35%)
BMI, kg/m^2	27 (24–31)	28 (25–31)	26 (23–31)
Arterial hypertension	135 (66%)	73 (73%)	62 (59%)
Type 2 diabetes	59 (29%)	30 (30%)	29 (28%)
Atrial fibrillation	97 (47%)	53 (53%)	44 (42%)
Stroke	17 (8%)	7 (7%)	10 (10%)
Previous cardiac surgery or intervention	32 (16%)	17 (17%)	15 (14%)
Ischaemic cardiomyopathy	79 (39%)	38 (38%)	41 (39%)
6MWD, m	292 (203–354)	296 (210–351)	290 (198–358)
New York Heart Association functional class			
II	83 (40%)	33 (33%)	50 (48%)
III	97 (47%)	52 (52%)	45 (43%)
IV	25 (12%)	15 (15%)	10 (10%)
Left ventricular ejection fraction, %	35 (29–45)	35 (29–45)	34 (28–46)
≤40%	136 (66%)	66 (66%)	70 (67%)
41–49%	35 (17%)	16 (16%)	19 (18%)
≥50%	33 (16%)	18 (18%)	15 (14%)
Serum creatinine, mg/dL	1·1 (0·9–1·6)	1·2 (1·0–1·6)	1·0 (0·84–1·3)
NT-proBNP, pg/mL	2216 (866–4945)	2037 (865–4757)	2303 (885–5434)
Inhibitors of the renin–angiotensin system	179 (87%)	87 (87%)	92 (88%)
β blocker	193 (94%)	92 (92%)	101 (96%)
Diuretics	189 (92%)	92 (92%)	97 (92%)
Aldosterone antagonist	134 (65%)	64 (64%)	70 (67%)
FACIT–PAL total score	39 (31–46)	40 (31–47)	39 (31–45)
KCCQ-OSS	45 (32–64)	41 (32–59)	52 (36–67)
HADS-A score	6 (3–9)	6 (3–9)	6 (3–9)
HADS-D score	6 (3–9)	5 (2–9)	6 (3–9)
MIDOS symptom intensity score	6 (4–9)	7 (4–10)	6 (3–8)
MIDOS wellbeing rating score	2 (2–3)	2 (2–3)	2 (2–3)
FACIT–SP12 score	30 (9)	31 (9)	29 (8)

Data are median (IQR), n (%), or mean (SD). Some percentages may not total 100% due to rounding. 6MWD=6-min walk distance. FACIT–PAL=Functional Assessment of Chronic Illness Therapy–Palliative Care. FACIT–SP12=Functional Assessment of Chronic Illness Therapy–Spiritual Well-Being 12. HADS-A=Hospital Anxiety and Depression Scale–Anxiety. HADS-D=Hospital Anxiety and Depression Scale–Depression. KCCQ-OSS=Kansas City Cardiomyopathy Questionnaire Overall Summary Score. MIDOS=Minimal Documentation System.

Table: **Baseline characteristics**

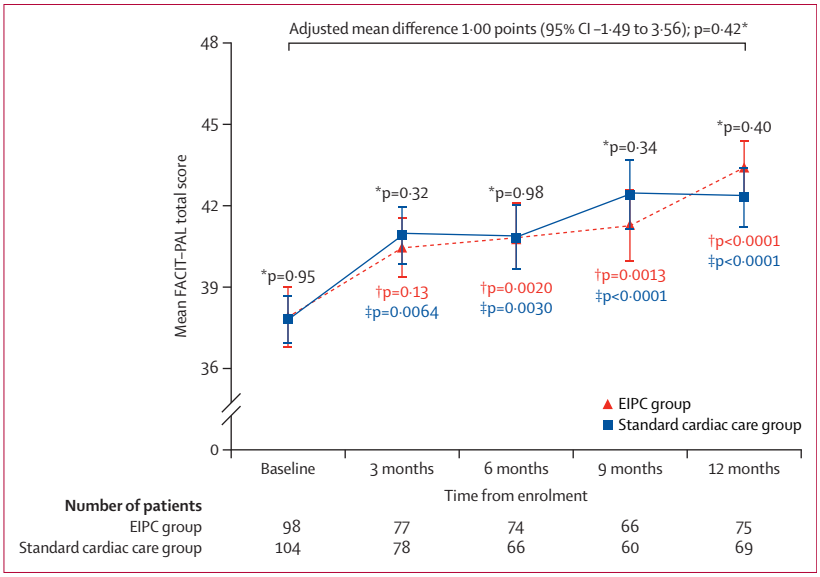

***Figure 2*: Changes in FACIT–PAL total scores**
Mixed model adjusted for corresponding baseline values and investigational sites. Whiskers show standard error. EIPC=early integration of palliative care. FACIT–PAL=Functional Assessment of Chronic Illness Therapy–Paliative Care. *Between-group comparison. †Within-group comparison with baseline for the EIPC group. ‡Within-group comparison with baseline for the standard cardiac care group.

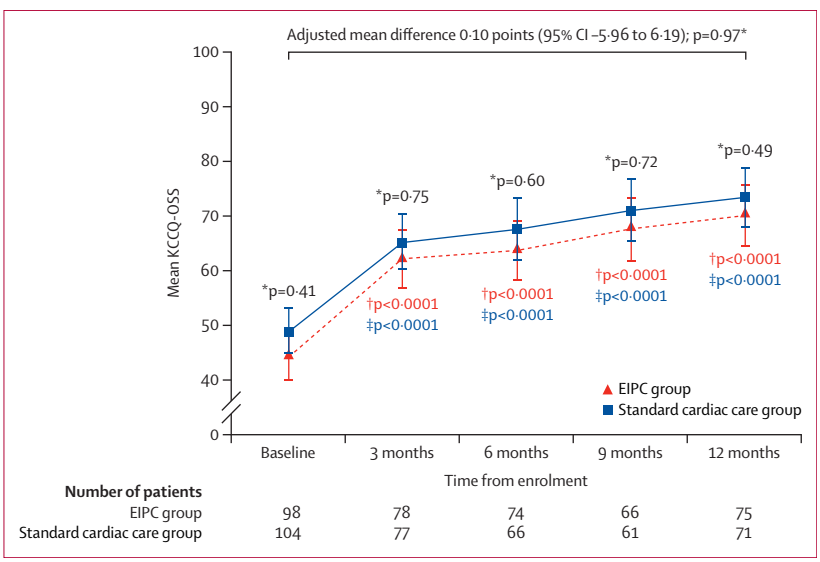

***Figure 3*: Changes in KCCQ-OSS**
Mixed model adjusted for corresponding baseline values and investigational sites. Whiskers show standard error. EIPC=early integration of palliative care. KCCQ-OSS=Kansas City Cardiomyopathy Questionnaire Overall Summary Score. *Between-group comparison. †Within-group comparison with baseline for the EIPC group. ‡Within-group comparison with baseline for the standard cardiac care group.

Overall, 70 (70%) patients in the EIPC group and 62 (59%) patients in the standard cardiac care group had any adverse events, with no significant differences between the groups (p=0·10; appendix p 8).

Discussion

In this open-label trial in patients with symptomatic, non-terminal heart failure, additional EIPC did not provide a significant advantage over standard cardiac care alone in enhancing health status and mood, apart from for spiritual wellbeing, which was significantly improved for those in the EIPC intervention group. However, this difference was not significant between the groups at 12 months. Furthermore, no significant differences were observed in hospitalisation or mortality rates between the two management strategies.

The absence of significant benefits of integrating palliative care for enhancing health status and mood among patients with heart failure could be attributed to the characteristics of our patient cohort. The majority of studies that show potential positive effects of palliative care on patients with heart failure have primarily focused on patients with advanced heart failure and a high predicted mortality rate.[14,22–25] Furthermore, a large proportion of these studies was conducted in an inpatient setting during episodes of acute decompensation.[22,26] By contrast, our study targeted patients with heart failure who were not in the terminal stages of their illness, which might explain the discrepant findings compared with previous studies.

The ENABLE CHF-PC study,[21] which similarly evaluated the effectiveness of EIPC in patients with heart failure who were not in the advanced stages of their illness, also did not report significant benefits from additional EIPC in terms of health status or mood, although it did show a clinically important improvement for pain intensity and interference with daily living for those receiving EIPC. Nonetheless, the cohort examined in the ENABLE CHF-PC study presented with relatively good baseline health status, evidenced by their KCCQ-clinical summary score and FACIT–PAL 14 item scores. This might suggest a ceiling effect, whereby the possibility for significant improvement was limited due to the participants' already favourable health conditions at the start of the trial.[21] Additionally, there was low adherence to the study protocol in ENABLE CHF-PC, with nearly half of the patients in the intervention group unable to attend the in-person palliative consultation, and 39% did not receive the full palliative care intervention as specified.[21] Moreover, the 16-week follow-up period in the ENABLE CHF-PC study might have been insufficient to observe significant improvements from additional EIPC in terms of health status or mood. These factors could have influenced the study's ability to evaluate the full potential benefits of EIPC.

In our trial, patients in the standard cardiac care group received regular follow-ups at 3-month intervals throughout a 1-year period. Additionally, supplementary telephone support was available from dedicated heart-failure nurses for all participants, regardless of their randomly assigned group, whenever further help or reassurance with medication was needed. These nurses also provided education about the condition and ensured adherence to medical regimens. This approach might have incorporated elements typically associated with general palliative care interventions, potentially blurring the distinct benefits of EIPC in improving health status and mood among patients with heart failure. However, the significant improvements in

spiritual wellbeing, observed exclusively in the EIPC group, underscore its unique potential benefits.

The findings of our trial highlight the potential of optimising management of patients with heart failure alongside regular outpatient follow-ups in enhancing the health status and mood of patients who are not in the terminal stages of the disease, even though our participants had relatively poor baseline conditions, with high mean baseline NT-proBNP concentrations, a short 6-min walk distance, a mean left ventricular ejection fraction of 35%, and poor to fair baseline KCCQ-OSS. Furthermore, our results support integrating palliative care with standard management of patients with heart failure to enhance overall patient care. This integration shows potential to enhance spiritual wellbeing, as evidenced in our study, and to reduce pain and daily living interference, as shown in the ENABLE CHF-PC study.

In the CASA trial,[27] the integration of palliative care into a comprehensive collaborative care model was investigated for patients with chronic heart failure and reduced health status. This intervention included symptom management by a registered nurse and structured psychosocial care by a social worker, both operating under the guidance of a health-care team that included a primary care clinician, a palliative care specialist, and a cardiologist. Although the primary outcome did not show significant improvement in health status as measured by the KCCQ-OSS, significant improvements were noted in depressive symptoms and fatigue, by the Patient Health Questionnaire-9 and the Patient-Reported Outcomes Measurement Information System Fatigue 8a questionnaires.[27] These findings underscore the potential benefits of integrating palliative care elements into regular management of patients with heart failure, particularly in enhancing other crucial aspects of patient wellbeing for those not in the terminal stages of their illness.

These findings highlight the need to refine intervention strategies, enhance patient selection criteria, and adopt a more individualised approach that considers disease severity and patient preferences.[28] Moreover, our findings underscore the importance of ongoing research into the interplay between palliative care and broader management strategies for patients with heart failure.

As the EPCHF trial was conducted during the COVID-19 pandemic, maintaining participant motivation for the quarterly follow-ups became more challenging, which might explain the relatively high loss to follow-up rate of 22%. Unfortunately, the study was not designed to examine the effects of the COVID-19 pandemic, infection, or vaccination on the health status and mood of patients. Incorporating these additional data would have required substantial modifications to the electronic data collection platform, study protocol, and statistical plan, along with obtaining sponsor and ethical approvals. This was not feasible since the study had been ongoing for almost 1 year by the time COVID-19 became widespread, with many participants having already completed or nearly completed their 12-month follow-up.

Although the current study provides valuable insights, it also has several limitations that warrant consideration. First, the study was exclusively conducted in German centres with extensive expertise in managing patients with heart failure, potentially limiting the generalisability of its findings. Additionally, the trial was conducted in an unblinded manner due to the collaborative and multidisciplinary nature of the intervention involving both the EIPC and cardiology teams. Furthermore, despite the study's relatively long duration of 1 year, there is a possibility that this timeframe might not have been adequate to fully capture meaningful changes in patients' health status and mood. Conducting longer-duration studies could provide a more comprehensive assessment of additional effects of EIPC.

In this open-label trial of patients with symptomatic, non-terminal heart failure, additional EIPC did not significantly enhance health status and mood over standard cardiac care alone. However, significant improvement in spiritual wellbeing was observed solely in the EIPC group, despite the difference between groups being non-significant.

Contributors

LR, GN, and MUB conceptualised and designed the study. MUB obtained funding. MB, Y-NB, CÖ, and RK recruited patients. MB, MH, and MN collected data. MB wrote the first draft of the manuscript. MB and MUB performed the statistical analysis. RW, RPf, VT, BW, RPö, TS, GN, and MUB provided supervision and reviewed and edited the manuscript. LR, GN, and MUB accessed and verified the data. All authors had full access to all the data in the study, reviewed and edited the manuscript, approved the final version of the manuscript, and had final responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

Data sharing

Most of the data generated or analysed during this study are included in the appendix. All datasets used or analysed during the current study are available from the corresponding author on reasonable request.

Acknowledgments

This study received funding from the Federal Ministry of Education and Research, identified by grant number 01GY1704. We would like to express our gratitude to Jennifer Schmitz for her administrative support throughout the study. We also extend our thanks to the team members of the Institute for Medical Biometry, Informatics, and Epidemiology at the University of Bonn for their assistance and support in the preparation and execution of this work.

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