Evaluation and improvement of integrated cardiac care: efficient and effective care in patients with chronic coronary artery disease and chronic heart failure

Vester, M.P.M.

CHAPTER 3

INTEGRATED CARE FOR HEART FAILURE PATIENTS: WHO TO REFER BACK TO THE GENERAL PRACTITIONER? – ACCORDING TO THE "TRANSMURAL CARE OF HF PATIENTS MODEL (LTA)" AND ESC-GUIDELINES

M.P.M. Vester[1], S.L.M.A. Beeres[1], C.M.H.B. Lucas[2], P.E.J. van Pol[2], M.J. Schalij[1], T.N. Bonten [3], P.R.M. van Dijkman[1], L.F. Tops[1]

[1]Department of Cardiology, Leiden University Medical Center, Leiden, the Netherlands

[2]Department of Cardiology, Alrijne Hospital, Leiderdorp, the Netherlands

[3]Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, the Netherlands

Submitted

ABSTRACT

Objective: The number of patients with heart failure (HF) and corresponding burden of the health care system will increase significantly. The vertically integrated program, "Transmural care of HF Patients" (LTA) was initiated to manage the increasing prevalence of HF patients in primary and secondary care and stimulate integrated care. It is unknown how many HF patients are eligible for back-referral to GPs, which is important information for the management of integrated care. This study aims to evaluate patients for whom HF care can be referred from the cardiologist to the GP.

Design and methods: All patients registered with chronic HF in two different hospitals were included, subsequently 200 patients were randomly evaluated**.** The following patients were considered eligible for referral to the GP: 1/Stable HF patients with reduced left ventricular ejection fraction (LVEF), 2/Stable HF patients with a recovered LVEF and 3/Stable HF patients with a preserved LVEF.

Results: Of the 200 patients, 17% was considered eligible for referral to the GP. This group consisted of 5% patients with a reduced LVEF, 10.5% patients with recovered LVEF, and 1.5% patients with a preserved LVEF. Main indicators for HF care by cardiologist were: active cardiac disease other than HF (39.5%), recent admission for HF (29.5%) or a recent adjustment in HF medication (7.5%) .

Conclusion: Based on the integrated care program of the LTA and the ESC-guidelines, opportunities for improvement of long term HF care are indicated. These results can be used to keep healthcare for HF patients accessible in the future.

INTRODUCTION

It is expected that in developed countries the prevalence of HF will rise to more than 10%.(1) Due to the ageing population, and improved medical treatment, the number of patients with HF and corresponding expenditures will increase significantly.(2-5) The increasing burden on the healthcare system is an important topic on the political agenda: a minimum level of financial growth for primary and secondary care is allowed in the forthcoming years.(6, 7)

This emphasizes the need to deliver HF care efficiently. Several trials have demonstrated that effective coordination of HF care improves clinical outcomes.(8, 9) Most of these studies focus on the referral of an HF patient from a general practitioner (GP) to cardiologist, but not the reverse. To provide the right care for the right patient at the right time and to maintain healthcare accessible in the future, referral back to the GP is equally important as timely referral to a cardiologist.(10, 11) Also, the ESC-HF Association Standards states that the follow-up and monitoring of chronic HF patients is a neglected area of HF care with only a small amount of literature to guide medical professionals.(12) In response to the above-mentioned trend, the Netherlands Society of Cardiology (Nederlandse vereniging voor Cardiologie) supports national and regional vertically integrated cardiac care programs in the Netherlands.(13) A regional integrated care program is the "Transmural Care of Heart Failure Patients Model " (LTA), initiated by cardiologists, GPs, specialised HF nurses, patients and health insurers. This model, based upon the European Society of Cardiology (ESC) guidelines, aims to optimize the organisation of HF care among GPs and cardiologists and provide integrated care. (1, 14, 15) It provides directions for the transition to a long-term management model of stable HF by GPs. However, it is unknown how many and which HF patients are eligible for back-referral to GPs, which is important information for the delivery of integrated care.

So, the aim of the present study was to evaluate the potential percentage and characteristics of patients in whom HF care can be referred back from a cardiologist to a GP based on the implementation of the LTA and in line with the latest ESC guidelines.

METHODS

Patients

A cross-sectional study was performed in two centers. Center A is a university medical center, where various outpatient clinics are available for HF patients. It provides 'structured tertiary care' for HF patients who are referred by a cardiologist to assess additional tertiary treatment options.(16) Furthermore, it provides 'standard HF care' in an outpatient setting by general cardiologists. Center B is a large regional teaching hospital with a dedicated HF outpatient clinic supervised by HF cardiologists.

In the Netherlands, all treatments and diagnoses supplied by health services are coded according to a national financial coding system. Patients with chronic HF were identified with the diagnosis code '021.302', corresponding with ICD-10 I50, in the year 2015 (when the LTA was implemented). From each center, a random sample of 100 patients was drawn. Data were collected from the departmental cardiology information system (EPD Vision; Leiden University Medical Center, The Netherlands, and Xcare; Nexus Nederland).(17) The following clinical characteristics were collected and analysed: age, gender, HF etiology, comorbidities, cardiac history, clinical characteristics, and laboratory results.

Transthoracic echocardiographic images of the patients were digitally stored in cine-loop format and analysed using commercially available software (GE Vingmed Ultrasound AS, Horten, Norway; EchoPAC version 112.0.1). The Simpson's biplane method was used for assessment of the left ventricular ejection fraction (LVEF) from the apical 2- and 4-chamber views.(18) The present study was approved by the Ethical board of the University of Leiden, written informed consent was waived for this retrospective data analysis.

Definitions

The following definitions were used to determine whether patients were eligible for referral to a GP or if treatment by a cardiologist was deemed necessary.(1, 14) This was based on the LTA and is in line with the 2016 ESC guidelines.

The following patients were eligible for back referral to GP:

- Stable HF, no active cardiac disease, optimal (medical) treatment, reduced LVEF. In particular an LVEF of 40-50% according to the latest ESC guidelines.
- Stable HF, no active cardiac disease, recovered LVEF (>50%)
- Stable HF, no active cardiac disease, optimal (medical) treatment, preserved LVEF
- HF, palliative setting

For the following patients treatment by a cardiologist is recommended:

- Unstable HF-related symptoms
- Stable HF, active cardiac disease, LVEF<50%
- Stable HF, active cardiac disease, LVEF>50%
- Stable HF, no active cardiac disease, LVEF<40% or comorbidity

'Unstable HF' was defined as a hospitalization within the last 12 months either due to decompensated HF or a cardiac intervention or a significant change in HF medication (Angiotensin-Converting-Enzyme inhibitor, Angiotensin-II Receptor Blocker, BetaBlocker or a MineralCorticoid Antagonist) in the last 6 months. An active cardiac disease was defined as: valvular disease, pulmonary hypertension, congenital heart defects, inherited cardiomyopathy, an invasive treatment for arrhythmias within the last 12 months or implantation of a cardiac device (this included a pacemaker (PM), an implantable cardioverter-defibrillator (ICD), a cardiac resynchronization therapy device (CRT-P or CRT-D). Comorbidities were defined according to the LTA, including but not limited to severe renal or pulmonary disease.

Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Science (SPSS) software version 23.0 (IBM, Armonk, NY, USA). All continuous data were normally distributed. Continuous data are reported as mean ±SD or SEM where appropriate, and categorical data as frequencies and percentages. Differences in baseline and clinical characteristics between patients were assessed using the Student *t*-test and Chi-square test. A p-value <0.05 was considered statistically significant, and all tests were 2-sided.

RESULTS

Baseline characteristics

A total of 1923 patients were identified, of which a random sample of 200 unique patients (100 patients in each center) was drawn for the analyses of medical files. Baseline characteristics are summarized in Table 1. Patients from Center A were predominantly male, significantly younger (66±15 years vs. Center B; 78±11 years, P<0.005) and had a lower LVEF compared with patients in center B (Center A; 38±11% vs. Center B; 44±14%, P<0.005). In both centers, almost half of the patients (Center A; n=45 (45%) vs. Center B; n=43 (43%)) had an ischemic etiology of their HF. More patients in Center B had atrial fibrillation as comorbidity (Center A; n=42 (42%) vs. Center B; n=58 (58%), P=0.024). There was a significant difference in implanted devices between the two centers. More patients in Center A had an ICD (Center A; n=20 (20%) vs. Center B; n=5 (5%), P<0.005) or a CRT-D, (Center A; n=22 (22%) vs. Center B; n=9 (9%), P <0.011). Patients in Center A had a better functional capacity according to the NYHA

classification (P<0.005) and had a better renal function (P=0.057). The prescribed HF medication was similar among both centers.

Table 1. Baseline characteristics

	Total (n=200)	Center A (n = 100)	Center B (n = 100)	P value*
Age, years	72 ±15	66 ±15	78 ±11	<0.005
Gender, n (%)				0.046
Male	114 (57%)	64 (64%)	50 (50%)	
Heart failure aetiology, n (%)				
Ischemic cardiomyopathy	88 (44%)	45 (45%)	43 (43%)	0.766
Non-ischemic cardiomyopathy	110 (55%)	55 (55%)	55 (55%)	1.000
Not established	2 (1%)	0 (0%)	2 (2%)	<0.005
Cardiac history, n (%)				
Myocardial infarction	55 (28%)	30 (30%)	25 (25%)	0.428
Revascularisation(PCI or CABG)	74 (37%)	39 (39%)	35 (35%)	0.558
Atrial fibrillation	100 (50%)	42 (42%)	58 (58%)	0.024
Surgery for valvular disease	27 (14%)	15 (15%)	12 (12%)	0.535
Device implantation				<0.005
PM	26 (13%)	9 (9%)	17 (17%)	0.093
ICD	25 (13%)	20 (20%)	5 (5%)	<0.005
CRT-P	1 (1%)	1 (1%)	0 (0%)	0.316
CRT-D	31 (16%)	22 (22%)	9 (9%)	0.011
LVEF (%)	41 ±13	38 ±11	44 ±14	<0.005
NYHA functional class, n				
I	67 (34%)	45 (45%)	22 (22%)	<0.005
II	90 (45%)	43 (43%)	47 (47%)	0.570
III/IV	41 (21%)	11 (11%)	30 (30%)	<0.005
N/A	2 (1%)	1 (1%)	1 (1%)	1.000
Systolic blood pressure (mmHg)	124 ±21	122 ±20	126 ±22	0.310
Diastolic blood pressure (mmHg)	72 ±10	74 ±10	73 ±11	0.448
ECG				
QRS duration (ms)	128 ±36	134 ±36	122 ±35	0.306
Heart rate (bpm)	72 ±14	71 ±14	74 ±13	0.235
Co-morbidity				
Hypertension	84 (42%)	41 (41%)	43 (43%)	0.774
Diabetes	42 (21%)	17 (17%)	25 (25%)	0.165
COPD	29 (15%)	11 (11%)	18 (18%)	0.160
PHT	37 (19%)	26 (26%)	11 (11%)	0.006

Table 1. Continued

	Total (n=200)	Center A (n = 100)	Center B (n = 100)	P value*
Laboratory results				
Haemoglobin (mmol/L)	8 ±6	8 ±3	7 ±3	0.800
Creatinin (umol/L)	110 ±54	99 ±52	121 ±53	0.057
Heart failure medication (n, %)				
ACEi/ARB	146 (73%)	74 (74%)	72 (72%)	0.750
Betablocker	163 (82%)	79 (79%)	84 (84%)	0.363
MRA	63 (32%)	28 (28%)	35 (35%)	0.287
Diuretics	133 (67%)	63 (63%)	70 (70%)	0.294

Continuous data are presented as mean (±SD), categorical data are presented as numbers (%). *P value between Center A and Center B.

ICD = implantable cardioverter defibrillator; PM = Pacemaker; CRT-D = Cardiac resynchronization therapy defibrillator; CRT-P = Cardiac Resynchronization Therapy Pacemaker; NYHA = New York Heart Association; LVEF = Left Ventricular Ejection Fraction; ECG = electrocardiography; COPD = chronic obstructive pulmonary disease; PHT = Pulmonary Hypertension; ACEi = angiotensin-converting-enzyme inhibitor; ARB = angiotensin II receptor blockers; MRA = Mineralocorticoid receptor antagonist

Potential substitution

According to the LTA criteria, a substantial amount of patients (17%) was eligible for follow-up by GP (Figure 1). Of all patients, 5% had stable HF with a reduced LVEF; 10.5% of patients had stable HF with a recovered LVEF and 1.5% of patients had HF with a preserved LVEF. None of the analysed patients were in a palliative setting. No significant differences were observed in the indications for back referral to the GP between the two centers. (Table 2)

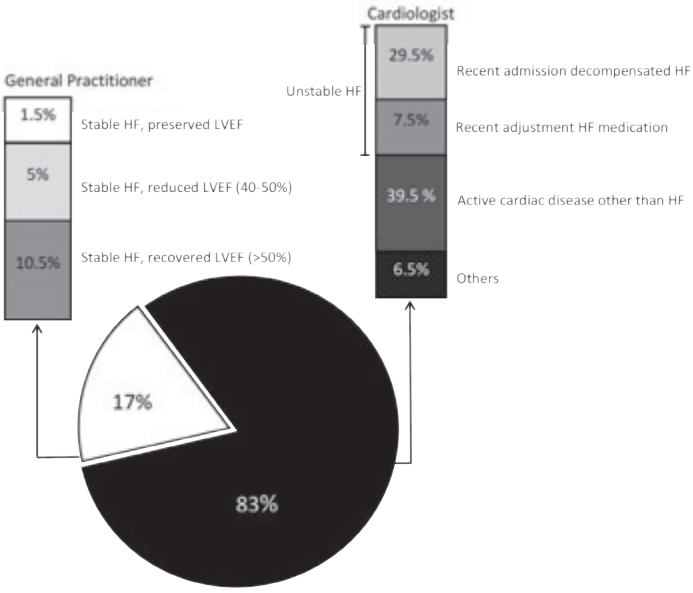

Figure 1. Overview of patients who were eligible for referral to the general practitioner (17%) and for who treatment by cardiologist was justified (83%) based on the "Transmural Care of Heart Failure Patients Model " and in combination with the latest ESC guidelines.
'Others' includes a comorbidity or a left ventricular ejection fraction <40%. HF = Heart Failure; LVEF = Left Ventricular Ejection Fraction

Table 2. Subdivision of heart failure patients based on recommendations of the LTA

	Total (n=200)	Center A (n = 100)	Center B (n = 100)	P-value
Potential substitution to GP				***0.559***
1. Stable heart failure, no active CD, reduced LVEF (40-50%)	10 (5.0%)	6	4	0.516
2. Stable heart failure, no active CD, recovered LVEF (>50%)	21 (10.5%)	9	12	0.489
3. Stable heart failure, no active CD, preserved LVEF	3 (1.5%)	2	1	0.561
Indications follow-up at cardiologist				***0.068***
4. Unstable heart failure	74 (37.0%)	30	44	0.040
5. Stable heart failure, active CD, LVEF <50%	53 (26.5%)	34	19	0.016
6. Stable heart failure, active CD, LVEF >50%	26 (13.0%)	12	14	0.674
7. Stable heart failure, no active CD, LVEF <40% or a comorbidity	13 (6.5%)	7	6	0.774

No significant differences were observed. Unstable heart failure was the main indication for follow-up at secondary care in Center B, whereas an active cardiac device was the main indication in Center A.
GP = General Practitioner; CD = Cardiac Disease; LVEF = Left Ventricular ejection fraction

Follow-up by cardiologist

A total of 83% of the patients had an indication for follow-up by a cardiologist (Figure 1). The majority of these patients had unstable HF (37%) or the presence of active cardiac disease (39.5%). In 6.5% of the patients, the indication for follow-up by a cardiologist was an LVEF <40% or comorbidity. Comorbidities included COPD, renal failure, Duchenne's disease, post-radiation therapy, or permanent atrial fibrillation.

Figure 2 summarizes the indications for follow-up by cardiologist and details the reason for 'unstable HF' and the various cardiac diseases, in the different centers. In both centers, the total number of patients with an indication for follow-up by a cardiologist was equal (Center A and Center B, n=83 (83%)). However, some indications for follow-up by a cardiologist were different among the centers. (Table 2.) First, the amount of patients with unstable HF was lower in Center A than in Center B (Center A; n=30 (30%) vs. Center B; n=44 (44%), P=0.040) and second, an active cardiac disease with a LVEF<50% was more often present in Center A than in Center B (A; n=34 (34%) vs. B; n=19 (19%) , P=0.016).

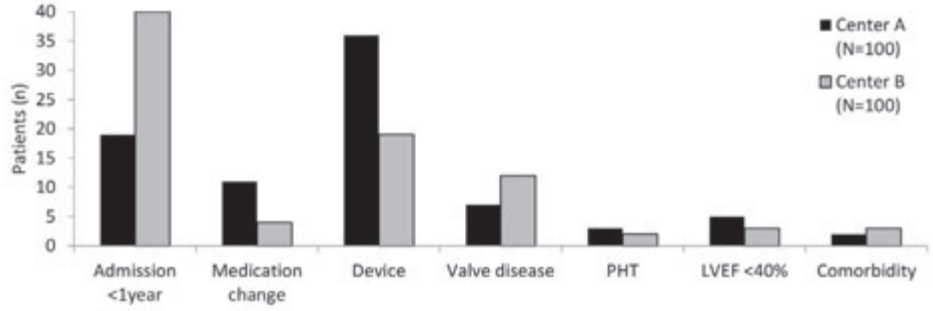

Figure 2. The amount of patients and main indication for follow-up at cardiologist in Center A (N = 83) and in Center B (N = 83) *LVEF = Left ventricular Ejection Fraction.*

DISCUSSION

The key finding of this study was that, based on an integrated care guideline (LTA and the ESC guidelines), 17% of HF patients seen in either a regional hospital or tertiary care center can be referred back to the general practitioner.

Management of HF

The potential to refer 17% of HF patients back to the GP is an important opportunity to further optimize HF integrated care and to deal with the increasing number of HF patients referred to the hospital. Our findings are supported by previous studies. The Northstar-study, a multi-center randomized clinical controlled trial, included clinically stable HF patients in an outpatient setting and allocated them equally to follow-up in the HF clinic or in primary care. It appeared that clinically stable HF patients, on optimal medical therapy can be safely managed in primary care with no additional benefit from long-term follow-up in a specialized HF clinic.(19) In the present study, patients who were hospitalized either due to HF or a cardiac intervention within the past 12 months or who had a significant change in HF medication within the past 6 months were considered 'unstable'. In the Northstar-study patients had at baseline a mean LVEF <35% and approximately 43% of the patients were admitted within the past 12 months. As patients in the present study had an LVEF >35% at baseline and only 29,5% were admitted within the past 12 months, it might imply that the current patient cohort is more stable, for which it might be even safer to refer the patients back to primary care.

Similar results were found in the COACH-2-study, a multi-center randomized controlled trial, in which 189 clinically stable HF patients were randomized and equally allocated to primary care or a specialized HF clinic. (20) Baseline characteristics of this study population were comparable to our population. The study showed that long-term follow in a specialized HF clinic was not superior to follow-up in primary care. Furthermore, the importance of integrated care in providing HF care during the unpredictable clinical course of HF patients was underlined. This aspect of HF care is also emphasized in the LTA, as the LTA strengthens the cooperation between care providers thereby creating a continuum of care.

Also, the study of de la Porte and co-workers confirmed the incremental value of collaboration between cardiologist and GP.(21) However, they observed a reduction in HF readmissions and mortality by an intensified HF management program, compared with usual care. A possible explanation for this finding can be the functional status of the patients. All patients were in NYHA class III or IV, whereas most (45%) of the patients in the current study were functioning in NYHA class II. This suggests that patients with a worse condition benefit more from these intensified HF programs.

Integrated care model

Worldwide healthcare expenditures are increasing rapidly. During the last decades, strategies to maintain access and sustainability of the healthcare systems and controlling rising healthcare expenditures have become important subjects on every governmental agenda.(6, 22) One strategy is to reduce fragmentation in healthcare delivery and increase collaboration and coordination among healthcare professionals. This can be established by working with an integrated care system. Integrated care systems can be understood as an organizing principle for coordinated care delivery where the needs of the patient are the central focus.(23) A way to describe integrated care is in horizontal integration and vertical integration. Horizontal integration happens when health care providers at the same stage of the health system collaborate. (24) Vertically integrated care is defined as the integration of care across different healthcare facilities at different stages in the process of delivering care. (25, 26) Multiple studies show the benefits of vertical integration in healthcare delivery, such as effective clinical care, a better communication process and increased collaboration.(27-30) It appears that successful integrated care programs strengthen the role of primary care. (31) The LTA accommodates the above as it provides clear care pathways for long-term integrated HF management between HF nurses, cardiologists and GPs. With the expected increase of HF prevalence, it is equally important to maintain access in hospitals for the HF patients who really need specialist care. The LTA provides guidance and more awareness to refer stable HF patients back from the cardiologist to GP. As is stated in the ESC-HF Association Standards, HF management should be a network of care pathways for the patient. (12, 19, 21, 32) With the implementation of the LTA, a network with close collaboration and coordination between healthcare providers is established and a continuum of HF care guaranteed.

Study Limitations

Several limitations should be acknowledged. The baseline characteristics were different among the two centers, one could expect this as center A is a tertiary care center and center B a secondary care center. However, only patients who received 'standard' HF care were randomly included. As a result, the potential effect of the LTA on a "real-world HF population" was analysed. What is also interesting is that despite the different baseline characteristics, the reasons for referral were not significantly different. It could either be that this is due to the small number of patients or it is a strong point; the results are both applicable on secondary as tertiary care centers . Another limitation is that follow-up data are not available yet. It will be interesting to study if the implementation of the LTA creates the intended awareness in HF care. Therefore a prospective study is needed to evaluate the true added value of the LTA regarding the referral of HF patients from cardiologist to GP.

Conclusion

This study demonstrates that based on the integrated care program in the LTA and the ESC guidelines, 17% of the HF patients currently treated by a cardiologist can be referred to the GP. The LTA creates awareness and indications in providing efficient HF care in the different phases of patients' disease. By creating a network of integrated care, high quality- and accessible HF care can be sustained in the near future.

REFERENCES

1. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2016;37(27):2129-200.
2. McMurray JJ, Stewart S. Epidemiology, aetiology and prognosis of heart failure. Heart. 2000;83:596-602.
3. Stewart S, MacIntyre K, Capewell S, McMurray JJV. Heart failure and the aging population: an increasing burden in the 21st century. Heart. 2003;89:49-53.
4. Conrad N, Judge A, Tran J, Mohseni H, Hedgecott D, Crespillo AP, et al. Temporal trends and patterns in heart failure incidence: a population-based study of 4 million individuals. The Lancet. 2018;391(10120):572-80.
5. Volksgezondheid Toekomst Verkenning (VTV). Toekomstige trend hartfalen door demografische ontwikkelingen: Rijksinstituut voor Volksgezondheid en Milieu (RIVM), ; 2018 [Available from: https://www.volksgezondheidenzorg.info/onderwerp/hartfalen/cijfers-context/trends#node-toekomstige-trend-hartfalen-door-demografische-ontwikkelingen.
6. Ministerie van Volksgezondheid WeSV. Onderhandelaarsakkoord medisch-specialistische zorg 2019 t/m 2022. In: Ministerie van Volksgezondheid Welzijn en Sport (VWS), editor.: Rijksoverheid; 2018.
7. Flinterman L, Groenewegen P, Verheij R. Zorglandschap en zorggebruik in een veranderde eerste lijn. Nivel; 2018.
8. McAlister FA, Stewart S, Ferrua S, McMurray JJ. Multidisciplinary strategies for the management of heart failure patients at high risk for admission: a systematic review of randomized trials. J Am Coll Cardiol. 2004;44(4):810-9.
9. Gustafsson F, Arnold JM. Heart failure clinics and outpatient management: review of the evidence and call for quality assurance. Eur Heart J. 2004;25(18):1596-604.
10. Cleland JGF, Cohen-Solal A, Aguilar JC, Dietz R, Eastaugh J, Follath F, et al. Management of heart failure in primary care (the IMPROVEMENT of Heart Failure Programme): an international survey. The Lancet. 2002;360(9346):1631-9.
11. Lucas CM, van Pol PE, Eysink Smeets JB, Niesing M, Verwey HF, Beeres SL. Heart failure in 2015: let's get organised! Neth Heart J. 2015;23(9):447-9.
12. McDonagh TA, Blue L, Clark AL, Dahlstrom U, Ekman I, Lainscak M, et al. European Society of Cardiology Heart Failure Association Standards for delivering heart failure care. Eur J Heart Fail. 2011;13(3):235-41.
13. NVVC Connect [cited 2021. Available from: https://www.nvvcconnect.nl/.
14. Burgers JS, van Laarhoven H, Van Pol PE, Valk MJM. Landelijke Transmurale Afspraak Hartfalen. De Nederlandse Vereniging voor Cardiologie (NVVC); 2015.
15. McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Bohm M, Dickstein K, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2012;33(14):1787-847.
16. Haeck ML, Hoogslag GE, Rodrigo SF, Atsma DE, Klautz RJ, van der Wall EE, et al. Treatment options in end-stage heart failure: where to go from here? Neth Heart J. 2012;20(4):167-75.
17. Nederlandse Zorgautoriteit. 2018 [Available from: http://www.opendisdata.nl.

18. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28(1):1-39 e14.

19. Schou M, Gustafsson F, Videbaek L, Tuxen C, Keller N, Handberg J, et al. Extended heart failure clinic follow-up in low-risk patients: a randomized clinical trial (NorthStar). Eur Heart J. 2013;34(6):432-42.

20. Luttik ML, Jaarsma T, van Geel PP, Brons M, Hillege HL, Hoes AW, et al. Long-term follow-up in optimally treated and stable heart failure patients: primary care vs. heart failure clinic. Results of the COACH-2 study. Eur J Heart Fail. 2014;16(11):1241-8.

21. de la Porte PW, Lok DJ, van Veldhuisen DJ, van Wijngaarden J, Cornel JH, Zuithoff NP, et al. Added value of a physician-and-nurse-directed heart failure clinic: results from the Deventer-Alkmaar heart failure study. Heart. 2007;93(7):819-25.

22. Rijksoverheid Ministerie van Volksgezondheid Welzijn en Sport. Naar beter betaalbare zorg. Rapport Taskforce Beheersing Zorguitgaven. In: Ministerie van Volksgezondheid Welzijn en Sport, editor. 2012.

23. Armitage GD, Suter E, Oelke ND, Adair CE. Health systems integration: state of the evidence. International journal of integrated Care. 2009;9.

24. Valentijn PP, Schepman SM, Opheij W, Bruijnzeels MA. Understanding integrated care a comprehensive conceptual framework based on the integrative functions of primary care. Int J Integr Care. 2013;13.

25. Valentijn PP, Schepman SM, WOpheij W, Bruijnzeels MA. Understanding integrated care a comprehensive conceptual framework based on the integrative functions of primary care. Int J Integr Care. 2013;13.

26. World Health Organization (WHO). Integrated care models: an overview. Denmark: WHO - Health Services Delivery Programme; 2016.

27. Verhaegh KJ, MacNeil-Vroomen JL, Eslami S, Geerlings SE, de Rooij SE, Buurman BM. Transitional care interventions prevent hospital readmissions for adults with chronic illnesses. Health Aff (Millwood). 2014;33(9):1531-9.

28. Melchiorre MG, Papa R, Rijken M, van Ginneken E, Hujala A, Barbabella F. eHealth in integrated care programs for people with multimorbidity in Europe: Insights from the ICARE4EU project. Health Policy. 2018;122(1):53-63.

29. Hollingworth SA, Donald M, Zhang J, Vaikuntam BP, Russell A, Jackson C. Impact of a general practitioner-led integrated model of care on the cost of potentially preventable diabetes-related hospitalisations. Prim Care Diabetes. 2017;11(4):344-7.

30. Harvey VLCG. The use of care pathways as tools to support the implementation of evidence-based practice. Journal of Interprofessional Care. 2009;14(4):311-24.

31. Dawda P. Integrated healthcare: the past, present and future. Integrated Healthcare Journal. 2019;1(1).

32. Bocchi EA, Cruz F, Guimaraes G, Pinho Moreira LF, Issa VS, Ayub Ferreira SM, et al. Long-term prospective, randomized, controlled study using repetitive education at six-month intervals and monitoring for adherence in heart failure outpatients: the REMADHE trial. Circ Heart Fail. 2008;1(2):115-24.