

The Medical Burden of Heart Failure: A Comparative Delineation with Cancer in Brazil

Dirceu Rodrigues de Almeida,¹ Antonio Carlos Pereira-Barretto,² Francisco Jose Forestiero,³ Juliana S. Nakamuta,³ André Bichels³

Universidade Federal de São Paulo,¹ São Paulo, SP – Brazil

Instituto do Coração do Hospital das Clínicas,² São Paulo, SP – Brazil

Novartis Biociências AS,³ São Paulo, SP – Brazil

Abstract

Background: Due to its poor prognosis and mortality rates, heart failure (HF) has been recognized as a malignant condition, comparable to some cancers in developed countries.

Objectives: To compare mortality from HF and prevalent cancers using data from a nationwide database in Brazil.

Methods: This was a descriptive, cross-sectional study using secondary data obtained from Brazilian administrative databases of death records and hospitalization claims maintained by the Ministry of Health. Data were analyzed according to main diagnosis, year of occurrence (2005-2015), sex and age group. Descriptive analyses of absolute number of events, hospitalization rate, mortality rate, and in-hospital mortality rate were performed.

Results: The selected cancers accounted for higher mortality, lower hospitalization and higher in-hospital mortality rates than HF. In a group analysis, HF showed mortality rates of 100-150 per 100,000 inhabitants over the period, lower than the selected cancers. However, HF had a higher mortality rate than each type of cancer, even when compared to the most prevalent and deadly ones. Regarding hospitalization rates, HF was associated with a higher risk of hospitalization when compared to cancer-related conditions as a group.

Conclusions: Our findings indicate that HF has an important impact on mortality, hospitalization and in-hospital mortality, comparable to or even worse than some types of cancer, representing a potential burden to the healthcare system.

Keywords: Cardiovascular Diseases/mortality; Heart Failure; Neoplasms/mortality; Brazil; Epidemiology; Mortality; Hospitalization; Answering Services/statistics & numerical data.

Introduction

More than 64 million people live with heart failure (HF) in the world.¹ Due to its progressive nature, HF is characterized by high mortality in the advanced phase, and its prognosis varies widely according to the population studied.¹ According to population-based studies, after the diagnosis of HF, survival estimates at 5 and 10 years are 50% and 10% respectively.²⁻⁶ The risk of mortality for HF patients is twice of people without the disease.⁷⁻⁹ A recent cohort study of patients diagnosed with HF from 2000-2017 in the United Kingdom reported only a modest improvement in survival in the 21st century.¹⁰⁻¹²

In a review published in 2002, McMurray and Stewart¹¹ conducted a comparison of HF mortality with different types of cancer. The authors showed that HF killed more patients than breast, prostate, bladder, bowel, and ovarian cancer. Only lung cancer was more malignant than HF.¹¹ Mamas et al.,¹² in a more recent review, showed that the statement presented by McMurray and Stewart remains valid until today, allowing us to conclude that HF is a more malignant disease than many types of cancer.¹² However, although the international literature is abundant in articles addressing HF mortality, there are no data to support that HF mortality is higher than cancer mortality in Brazil.

Mailing Address: Francisco Jose Forestiero

Av. Professor Vicente Rao, 90. Postal Code: 04706-900, Cidade Monções, São Paulo, SP – Brazil.

E-mail: francisco.forestiero@novartis.com

The primary objective of this study was to compare the number of in-hospital deaths due to HF and selected cancer diseases in Brazil between 2005 and 2015. Secondary objectives were to compare the number of hospital admissions due to HF and selected cancer diseases in Brazil between 2005 and 2015; and to compare in-hospital mortality rates from HF and selected cancer diseases in Brazil between 2005 and 2015.

Study design

This was a descriptive, cross-sectional study using secondary data obtained from the SIM (Mortality Information System)¹³ and the SIH (Hospital Information System) of the Information Technology Department of the Brazilian Ministry of Health.¹³ The SIH is an administrative database of data from hospitals of the Brazilian unified Health System (SUS), including admission data – authorization forms, demographics, hospitalization cause – length of stay and in-hospital mortality, which are used for health service and system planning and knowledge production in the field of public health.¹⁴ The SIM provides nationwide population-based data about mortality – main cause and secondary causes of death, and demographics, obtained from death certificates. As for SIH, these data help in planning of health services and programs.¹⁵

Both SIM and SIH are publicly available databases created and maintained by DATASUS.¹⁶ The analysis comprised a period of eleven years, of registries between 2005 and 2015 of individuals aged ≥ 45 years, age when cardiovascular disease is most diagnosed. Files containing anonymized data were downloaded directly from the DATASUS website in their original format. Data on hospitalization and death were retrieved from the SIH and SIM databases, respectively, of the 26 states and the Federal District in Brazil. Data cleaning and validation was conducted by the investigators to identify completeness and integrity of available data.

We considered the 10th International Classification of Disease (ICD-10) code for Heart Failure I50, and the most prevalent cancers: C16 stomach cancer, C18 colon cancer – grouped with C19 malignant neoplasm of recto sigmoid junction and C20 rectum cancer, C34 trachea, bronchi and lung cancer, C50 breast cancer (except for male cases of breast cancer for both death events and in-patient admissions), C53 cervix cancer and C61 prostate cancer.

Brazilian population projections were obtained from DATASUS website.¹⁶ These projections are obtained from the Brazilian Institute of Geography and Statistics

(IBGE) using methods described in the Brazilian National Population Projections by age and sex: 2000-2060.¹⁷ Estimates are calculated using data from the Brazilian 2010 Demographic Census and information of births and deaths obtained from official records.

Statistical analysis

The data were aggregated for calculations of mortality and hospitalization, in absolute numbers and rates, by disease and year of occurrence. Each event (hospitalization, death and in-hospital death) was coded according to the ICD-10 classification (after accounting for ill-defined or undefined causes of death) and the aggregated groups of causes were analyzed considering the year of occurrence (2005 to 2015).

For death events, a redistribution method of ill-defined causes of death (Chapter XVIII of the ICD-10 - Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified) was used as described by Soares et al.¹⁵ Undefined causes of death were redistributed using the proportion of each defined cause except for external causes (which were assumed to contribute to a small proportion of in death records). These reclassified death records were summed to the absolute number of deaths initially coded with eligible ICD-10 codes for the study.

Data were then descriptively compared year by year between selected diseases using graphs.

As a descriptive study, all data on death and hospitalization that met the eligibility criteria were organized and stored in a Microsoft Excel spreadsheet. Thus, sample size calculation was not applicable.

Results

Due to the nature of the study – a retrospective database study without patient-level data – information about participants is not disclosed.

Table 1 presents the absolute number of hospitalizations for different types of cancer and HF from 2005 to 2015. The frequency of hospitalization for HF was higher compared with various types of cancer.

Table 2 shows the number of patients who died during hospitalization for cancer or HF treatment.

We observed a higher number of in-hospital mortality for HF compared with selected types of cancer over the study period. Undefined causes of death contributed to an average of 8.13% of deaths in the period.

Table 1 - Absolute number of hospitalizations for different types of cancer and heart failure from 2005 to 2015

Selected diagnoses	Year										
	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
C16 Stomach cancer	14,550	14,861	14,440	13,154	14,119	15,395	16,552	17,604	18,770	19,983	20,673
C18-C20 Colorectal cancer	16,471	18,295	19,313	22,864	25,662	30,574	37,050	41,244	46,871	49,760	52,734
C34 Trachea, bronchi and lung cancer	11,558	12,481	12,996	12,408	13,725	14,982	15,515	16,916	18,075	19,366	20,113
C50 Breast cancer	25,111	25,804	27,208	27,833	29,405	31,742	33,375	37,450	41,607	43,395	45,565
C53 Cervix cancer	15,406	15,305	13,969	14,126	13,564	13,347	12,992	12,859	12,578	11,754	11,523
C61 Prostate cancer	14,224	13,388	13,938	17,659	19,850	21,985	23,852	25,669	26,685	27,593	29,549
I50 Heart Failure	277,168	265,628	248,010	242,094	241,536	236,827	232,277	216,834	210,346	198,370	192,181

Table 2 - Absolute numbers of in-hospital mortality from the selected diseases in each calendar year from 2005 to 2015

Selected diagnoses	Year										
	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
C16 Stomach cancer	3,038	3,220	3,330	3,140	3,594	3,695	3,768	4,060	4,276	4,455	4,308
C18-C20 Colorectal cancer	2,297	2,556	2,731	3,004	3,336	3,852	4,223	4,659	5,084	5,365	5,373
C34 Trachea, bronchi and lung cancer	3,275	3,567	4,185	4,027	4,617	5,034	5,230	5,671	6,141	6,500	6,541
C50 Breast cancer	1,968	2,163	2,467	2,709	2,940	3,270	3,494	3,822	4,160	4,292	4,438
C53 Cervix cancer	1,041	1,069	1,231	1,274	1,510	1,622	1,684	1,739	1,756	1,744	1,788
C61 Prostate cancer	1,196	1,273	1,501	1,734	2,060	2,322	2,553	2,654	2,932	3,135	3,161
I50 Heart Failure	22,517	24,238	24,440	24,682	25,616	26,457	27,422	26,264	26,713	26,059	25,004

Table 3 shows the percentage of in-hospital mortality of patients with HF and with different types of cancer. HF mortality has increased progressively in these eleven years. Patients with HF hospitalized for compensation had an average mortality in of 11.08%, higher than breast cancer (9.60%) and prostate cancer (10.32%) and lower than other types of cancer.

Discussion

Several authors have called attention to the fact that the mortality of HF patients is high and more pronounced than of patients with some types of cancer.^{13,14} In Brazil,

the mortality of patients with HF is also high, particularly when compared with mortality rates described in developed countries, but there are no data comparing mortality from HF with cancer in our country. In this article, we made this comparison using data from DataSUS.¹⁵⁻¹⁷

The comparative analysis of hospital admissions for HF with admissions for the most prevalent types of cancer revealed significantly higher numbers of patients hospitalized due to HF than cancer (Table 1). Besides, the number of patients who died from HF was significantly higher than those who died from different types of cancer (Table 2). In addition, considering in-hospital mortality,

Table 3 – Percentage of in-hospital mortality of patients with HF and with different types of cancer

Selected diagnoses	Year										
	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
C16 Stomach cancer	20.88	21.67	23.06	23.87	25.46	24.00	22.76	23.06	22.78	22.29	20.84
C18-C20 Colorectal cancer	13.95	13.97	14.14	13.14	13.00	12.60	11.40	11.30	10.85	10.78	10.19
C34 Trachea, bronchi and lung cancer	28.34	28.58	32.20	32.45	33.64	33.60	33.71	33.52	33.98	33.56	32.52
C50 Breast cancer	7.83	8.38	9.07	9.73	10.00	10.30	10.47	10.21	10.00	9.89	9.74
C53 Cervix cancer	6.76	6.98	8.81	9.02	11.13	12.15	12.96	13.52	13.96	14.84	15.52
C61 Prostate cancer	8.41	9.51	10.77	9.82	10.38	10.56	10.70	10.34	10.99	11.36	10.70
I50 Heart Failure	8.12	9.12	9.85	10.20	10.61	11.17	11.81	12.11	12.70	13.14	13.01

we may say that HF was more malignant than breast cancer and prostate cancers (Table 3), as mean mortality rate of patients hospitalized due to acute HF (11.08%) was higher than breast (9.60%) and prostate cancers (10.32%).

In Latin America, HF is the leading cause of hospitalization, with rehospitalization rates of 33%, 28%, 31%, and 35% at 3, 6, 12, and 24 to 60 months of follow-up, respectively.^{18,19} Despite treatment advances, HF still has a poor prognosis, with high mortality rates. Five-year mortality rate for HF was estimated at approximately 50%.²⁰ In Latin America, it is estimated a one-year mortality rate of 24.5%, and in-hospital mortality rate of 11.7%.¹⁹ Brazilian registry data indicate an in-hospital mortality rate of 12.6%.²¹

As shown in previous studies in developed countries,^{14,20,22} HF can be associated with worse outcomes than some types of cancer. Askoxylakis et al.,²⁰ conducted a systematic review of the literature and noted a five-year survival of approximately 43% for all cancer types and 26-52% for HF, showing that HF in some settings is as deadly as some cancers, and even worse as compared with cancers like breast cancer (73-89%), prostate cancer (50-99%) and colorectal cancer (43-63%).²⁰ Using a retrospective approach, Stewart et al.,²² identified that the annual incidence of first-ever hospitalization for HF was higher than for cancer in Sweden: 484 versus 373 (lung, colorectal, prostate, and bladder cancer combined) per 100,000 men and 470 versus 350 (lung, colorectal, bladder, breast, and ovarian cancer combined) per 100,000 among women aged > 20 years. The authors also observed that the 30-day and five-year mortality rates were comparable between

HF and cancer, and that during the 10-year follow-up period, HF was associated with more premature life-years lost than all common forms of cancer in men but not in women.²² Mamas et al.,¹² conducted an analysis of survival rate comparing HF with some forms of cancer. The authors' findings indicated that HF had significantly worse five-year survival rate (55.8%) than prostate cancer (68.3%) and bladder cancer (57.3%), but significantly better than lung cancer (8.4%) and colorectal cancer (48.9%). In women, HF mortality outcome was worse (49.5%) than breast cancer (77.7%), but better than colorectal cancer (51.5%), lung cancer (10.4%), and ovarian cancer (38.2%).¹⁴

Our data confirm the described in Latin America and in the world^{14,20,22} regarding high rates of mortality from HF as compared with some cancers. These data reinforce the need to recognize HF as a priority condition in Brazil, mainly by health system managers and policy makers, but also by the general population. Besides the magnitude of the disease burden in terms of deaths and hospitalizations, the decreasing rates observed in temporal series highlight that HF potentially responds to improvement in care with better outcomes that are relevant for both patients and the health care system, once hospitalization is the main cost driver in HF.^{22,23}

Since the data used in this analysis were representative of all the death certificates and hospitalization claims from the Brazilian public health care system during the 2005-2015 period, it is possible to assume that the findings are applicable to the national setting for mortality data and for the public health care system for hospital admission data.

It is important that physicians become aware of these data, to try to make an earlier diagnosis of HF and provide earlier treatment using the best evidence, and thereby modify the natural history of the disease.

It is worth remembering that the CONSENSUS study showed that, although it was possible to modify the course of HF, the mortality remained high (44%) in the control group in the first six months and in the first year (52%). The prescription of enalapril reduced mortality to 26% in the first six months and to 36% at the end of the first year.²³ With the introduction of beta-blockers, mineralocorticoid receptor antagonists, angiotensin receptor antagonists and, more recently an angiotensin receptor neprilysin inhibitor (ARNI), it is possible to substantially reduce the mortality of patients with insufficiently treated HF.²⁴⁻²⁶

An interesting point often discussed in Brazilian scientific meetings is the interpretation of the recent reduction in the number of hospitalizations for HF per year, as indicated by the SUS data. Some presentations interpret such decrease as a result of better management of the cases, without taking into account, however, the significant reduction in the number of SUS beds (Table 4) in recent years. With a smaller number of beds, physicians are pressured to admit only the most serious patient who will have the highest mortality, even with the best treatment available.

We can conclude that HF alone promotes more hospitalizations and deaths than some types of cancer. The mortality of patients with HF was higher than the one observed in patients with breast or prostate cancer, a result similar to other studies around the world. This concept of HF malignancy should be better

disseminated so that more attention would be paid to patients with the syndrome, as its prognosis varies with treatment (e.g. timing and dosage, use of neurohormonal blockers), according to national guidelines.

Limitations

The results of hospitalization and in-hospital mortality of the present study are probably not applicable to the private health care system, since the access to health care services, treatment patterns and epidemiological profile of patients are markedly different between both settings. The main limitation of this study is its retrospective approach based on administrative databases that were not specifically designed for the purposes of the study. For this reason, detailed clinical data about diagnosis and treatment were not available, limiting our ability to adjust for the comorbidity burden of HF, for example. Also, it was not possible to differentiate between HF with reduced and preserved ejection fraction. Another limitation was that it was not possible to use record linkage to combine HF- and cancer-related hospitalization and mortality data to identify unique patients. Another limitation of this study was the absence of patient-level longitudinal data that could allow further analysis including survival analysis, as previously performed by other researchers.^{14,20} Despite these limitations, both SIM and SIH databases have been widely used for epidemiological research in Brazil with valid and well-accepted results.^{15,16} These aspects can be further explored in futures studies conducted in Brazil, including HF cost studies, to provide greater knowledge about the clinical and economic burden of HF in the country.

Table 4 – Number of public hospital beds by geographic region in Brazil

Regions	2009	2020	Δ (difference)
North	29,984	30,357	373
Northeast	121,864	114,215	-7,449
Southeast	197,809	171,967	-25,842
South	74,277	72,947	-1330
Midwest	37,194	36,902	-292
Total	460,928	426,388	-34,540

Source: Estado de São Paulo, March 25th 2020

Conclusion

The results of this analysis indicate that HF causes a significant burden to the health care system and the society, in terms of mortality and hospitalization. This burden is comparable or even worse than that caused by some types of cancer. It is urgent that health managers, policy makers and the society need to prioritize the early diagnosis, prevention and treatment of HF, when deciding about resource allocation in the health care system

Author contributions

Conception and design of the research; Analysis and interpretation of the data; Writing of the manuscript; Critical revision of the manuscript for intellectual content: Almeida DR, Pereira-Barretto

References

- Bueno H, Moura B, Lancellotti P, Bauersachs J. The year in cardiovascular medicine 2020: heart failure and cardiomyopathies. *Eur Heart J*. 2021;42(6):657-70. doi: 10.1093/eurheartj/ehaa1061.
- Thorvaldsen T, Benson L, Dahlstrom U, Edner M, Lund LH. Use of evidence-based therapy and survival in heart failure in Sweden 2003-2012. *Eur J Heart Fail* 2016;18(5):503-11. doi: 10.1002/ehfj.496.
- Damman K, Valente MAE, Voors AA, Connor CM, Van Veldhuisen DJ, Hillege HL, et al. Renal impairment, worsening renal function, and outcomes in patients with heart failure: an updated meta-analysis. *Eur Heart J*. 2014;3(7):455-68. doi: 10.1093/eurheartj/ehz386
- Lee TT, Chen J, Cohen DJ, Tsao L. The association between blood pressure and mortality in patients with heart failure. *Am Heart J*. 2006; 151(1):76-83. doi: 10.1016/j.ahj.2005.03.009.
- Elkayam U, Tasissa G, Binanay C, Stevenson LW, Ghlorgiad M, Warnica JW, et al. Use and impact of inotropes and vasodilator therapy in hospitalized patients with severe heart failure. *Am Heart J*. 2007;153(1):98-104doi: 10.1016/j.ahj.2006.09.005.
- Hashim T, Sanan K, Revilla-Martinez M, Morgan CJ, Tallaj JA, Pamboukian SV, et al. Clinical characteristics and outcomes of intravenous inotropic therapy in advanced heart failure. *Cir Heart Fail*.2015;8(5):880-6. doi: 10.1016/j.ahj.2006.09.005v
- Roger VL. Epidemiology of Heart Failure. *Circ Res*. 2013; 113(6): 646-59. doi: 10.1161/CIRCRESAHA.113.300268
- Cowie MR, Wood DA, Coats AJ, Thompson SG, Suresh V, Poole-Wilson PA, Sutton GC. Survival of patients with a new diagnosis of heart failure: a population based study. *Heart*. 2000;83(5):505-10. doi: 10.1136/heart.83.5.505.
- Mosterd A, Cost B, Hoes AW, de Bruijne MC, Deckers JW, Hofman A, Grobbee DE. The prognosis of heart failure in the general population: The Rotterdam Study. *Eur Heart J*. 2001;22(15):1318-27. doi: 10.1053/ehj.2000.2533.
- Taylor CJ, Ordóñez-Mena JM, Roalfe AK, Lay-Flurrie S, Jones NR, Marshall T, Hobbs R. Trends in survival after a diagnosis of heart failure in the United Kingdom 2000-2017: population based cohort study. *BMJ*. 2019;364(364): 1223. doi: 10.1136/bmj.1223
- McMurray JVV, Stewart S. The burden of heart failure. *Eur Heart J*. 2002; 4(SupplD):50-8.
- Mamas MA, Sperrin M, Watson MC, Coutts A, Wilde K, Burton C, et al. Do patients have worse outcomes in heart failure than in cancer? A primary care-based cohort study with 10-year follow-up in Scotland. *Eur J Heart Fail*. 2017;19(9):1-10. doi: 10.1002/ehf.822.
- Bittencourt SA, Camacho LAB, Leal MC. O Sistema de Informação Hospitalar e sua aplicação na saúde coletiva Hospital. *Cad Saude Publica*. 2006;22(1):19-30. doi: 10.1590/s0102-311x2006000100003.
- Haraki CAC, Gotlieb SLD, Laurenti R. Confiabilidade do Sistema de Informações sobre Mortalidade em município do sul do Estado de São Paulo. *Rev Bras Epidemiol*. 2005;8:19-24.
- Soares DA, Gonçalves MJ. Mortalidade cardiovascular e impacto de técnicas corretivas de subnotificação de óbitos mal definidos. *Rev Panam Salud Pública*. 2012;32(3):199-206. doi: 10.1590/s1020-49892012000900005
- Brasil.Ministério da Saúde. DATASUS Tecnologia da Informação a Serviço do SUS. [Citado em 2021 set 12] Disponível em: <http://tabnet.datasus.gov.br/cgi/tabcgi.exe?ibge/cnv/projpopuf.def>
- Instituto Brasileiro de Geografia e Estatística. (IBGE). [Citado em 2021 set 13]. Disponível em: <https://www.ibge.gov.br/estatisticas/sociais/populacao/9109-projecao-da-populacao.html?>
- Bocchi EA. Heart failure in South America. *Curr Cardiol Rev*. 2013;9(2):147-56. doi: 10.2174/1573403x11309020007.
- Ciapponi A, Alcaraz A, Calderón M, Matta MG, Chaparro M, Soto N, Bardach A. Burden of Heart Failure in Latin America: A Systematic Review and Meta-analysis. *Rev Esp Cardiol* 2016;69(11):1051-60. doi: 10.1016/j.rec.2016.04.054
- Askoxyllakis V, Thieke C, Pleger ST, Most P, Tanner J, Lindel K, et al. Long-term survival of cancer patients compared to heart failure and stroke: A systematic review. *BMC Cancer*. 2010;10:105. doi: 10.1186/1471-2407-10-105.
- Albuquerque DC de, Souza Neto JD de, Bacal F, Rohde LEP, Bernardez-Pereira S, Berwanger O, Almeida DR. I Brazilian Registry of Heart Failure - Clinical Aspects, Care Quality and Hospitalization Outcomes. *Arq Bras Cardiol*. 2015;104(6):433-42. doi: 10.5935/abc.20150031.

AC, Forestiero FJ, Nakamuta JS, Bichels A. Obtaining financing: Bichels A.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors.

22. Stewart S, Ekman I, Ekman T, Oden A, Rosengren A. Population impact of heart failure and the most common forms of cancer: A Study of 1 162 309 Hospital Cases in Sweden (1988 to 2004). *Circ Cardiovasc Qual Outcomes*. 2010;3(6):573–80. doi: 10.5935/abc.20150031.
23. Bui AL, Horwich TB, Fonarow GC. Epidemiology and risk profile of heart failure. *Nat Rev Cardiol*. 2011;8(11):30–41. doi: 10.1038/nrcardio.2010.165.
24. The CONSENSUS trial study group: Effects of enalapril on mortality in severe congestive heart failure. Results of the Cooperative North Scandinavian Enalapril Study (CONSENSUS). *N Engl J Med*. 1987;316(23):1420-35. doi: 10.1056/NEJM198706043162301.
25. Sociedade Brasileira de Cardiologia (SBC), Rohde LEP, Montera MW, Bocchi EA, Clausell NO, Albuquerque DC, Rassi S, et al. Diretriz Brasileira de Insuficiência Cardíaca Crônica e Aguda. *Arq Bras Cardiol*. 2018;111(3):439-539. doi: 10.5935/abc.20180190.
26. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, 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. *Eur Heart J*. 2016;37(27):2129-200. doi: 10.1093/eurheartj/ehw128.

