BURDEN OF MORTALITY IN PATIENTS WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION – A LITERATURE REVIEW

PCV6

Gogna S[1], Agrawal R[1], Jindal R[1], Proudfoot C[2]

[1]Novartis Healthcare Pvt. Ltd., Hyderabad, India, [2]Novartis Pharma AG, Basel, Switzerland

BACKGROUND

- Heart failure (HF) is a complex clinical syndrome in which the heart is unable to pump sufficient blood to meet the metabolic demands of tissues and organs, or only at the expense of increased filling pressures[1,2].
- HF is broadly categorised into HF with reduced ejection fraction (HFrEF - left ventricular ejection fraction [LVEF] <40%) and HF with preserved ejection fraction (HFpEF - LVEF ≥50%)[1,3].
- There are differences in patient characteristics, aetiology, and available treatments across the LVEF spectrum.
- This underlines the need to understand mortality rates and mode of death specifically in HFpEF.

OBJECTIVE

- A literature review was conducted in order to understand the burden of mortality in patients with HFpEF.

METHODS

- A literature review with a predefined methodology and inclusion criteria was performed (**Table 1**).
- Mortality rates and its causes were compared among all the HF phenotypes.

Table 1: Literature sources and inclusion criteria used for the review

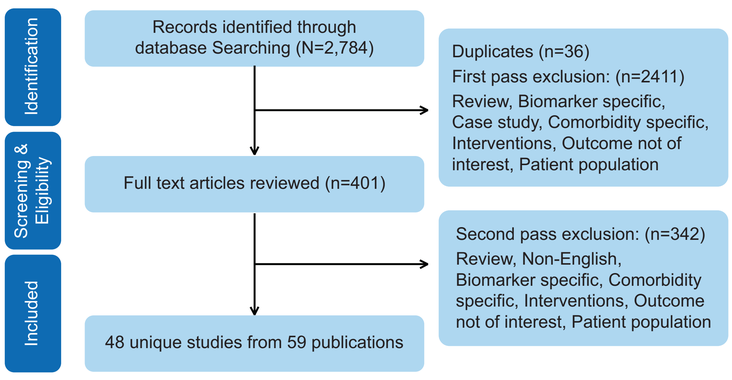
Sources of literature	
Databases	Embase® and MEDLINE®
Other sources	Bibliographic search
Inclusion	
Population	Adult (aged ≥18 years) patients with HFpEF
Intervention/ Comparator	Not applicable
Outcomes	Mortality: • All cause death • CV death • Non CV death • HF death • Sudden death
Study designs	Observational studies
Limits	
Language	English
Search timeframe	January 2012 to 4 September 2018
Country	No limits

CV: cardiovascular; HFpEF: heart failure with preserved ejection fraction

RESULTS

- From 2,784 publications, 264 were selected for full-text screening and 48 unique studies met the inclusion criteria (**Figure 1**).
- The mean age ranged from 54.2 to 84.0 years and the proportion of females ranged from 8.9 to 76.2% in the included studies.
- Of 48 included studies, 39 also compared mortality estimates across LVEF subgroups.

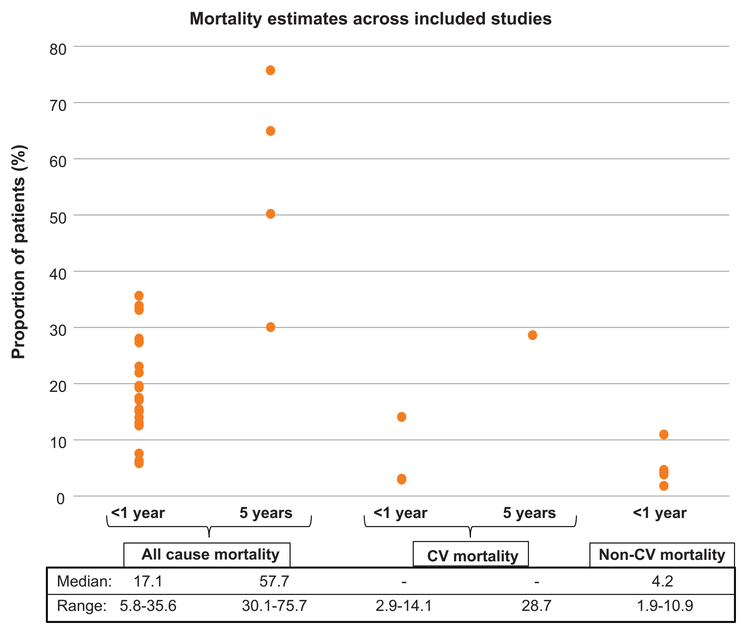
Figure 1: Study flow diagram



Mortality estimates

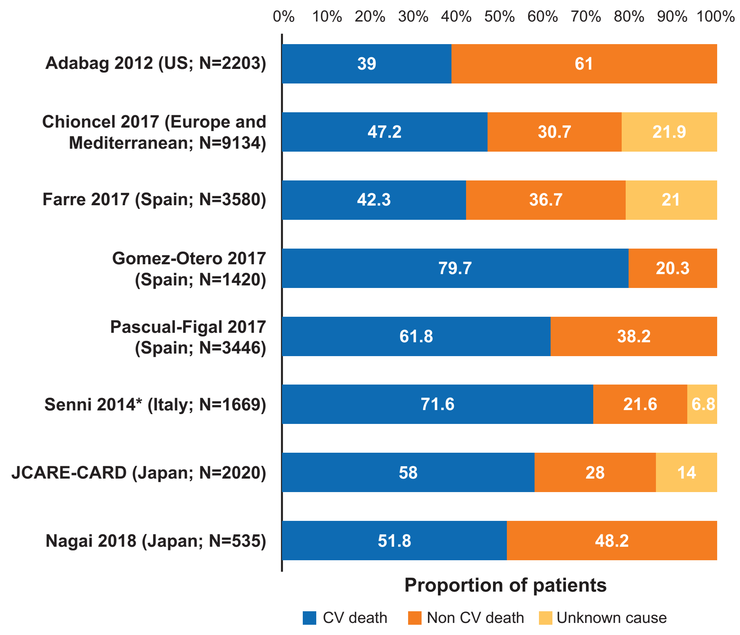
- Mortality estimates (all-cause, CV and non-CV) varied largely across the included studies as shown below (**Figure 2**). The considerable variability across included studies may be due to variations in baseline comorbidities, age and baseline characteristics of the patient population and sample size.
- Estimates (proportion of patients) for all cause, CV, and non-CV mortality at 1 year follow-up among HFpEF patients ranged considerably, from 5.8-35.6%, 2.9-14.1%, and 1.9-10.9%, respectively.
- HF mortality and sudden deaths were also reported in 9 studies and 5 studies, respectively. The rates of HF mortality and sudden deaths at 1 year follow-up ranged from 0.7 - 8.5% and 3.8 - 11.0%, respectively.

Figure 2: Scatter plot showing mortality estimates across included studies



Each point in the figure denotes proportion of patients died in particular study

Figure 3: Proportion of CV and non-CV related deaths



*proportion of unknown-cause deaths in this study were assumed

Classification of death in HFpEF

- The majority of deaths in HFpEF patients are due to CV causes as illustrated in **Figure 3**.

Comparison of mortality across HF phenotypes

- Majority of studies (10 of 11 studies) reported higher CV mortality in HFrEF compared to HFpEF (**Table 2**). Statistically significant differences were shown in 6 of 11 studies.
- In contrast, non-CV mortality was found to be higher in HFpEF patients (6 of 7 studies, significant difference in 3) as shown in **Table 2**.
- For all-cause mortality, there was less difference between HFpEF and HFrEF, as higher non-CV mortality in HFpEF and higher CV mortality in HFrEF tended to equalize, although some studies reported somewhat higher rates in HFrEF (**Table 3**).
- HF mortality and sudden deaths were also observed to be higher in HFrEF (HF mortality: 6/8 studies; sudden death: 4/5 studies) compared to HFpEF. Statistical significance was observed in 2 and 3 studies, respectively.

Table 2: Proportion of patients (%) with CV and Non-CV mortality rates across HF phenotypes

Study name	HFrEF (%)	HFpEF (%)	Study name	HFrEF (%)	HFpEF (%)	Study name	HFrEF (%)	HFpEF (%)
CV Mortality								
Chioncel 2017	4.7	3	Ushigome 2015 (CHART 1)	18	17	Pascual-Figal 2017	26.4	17.3
Gomez-Otero 2017	2.1	3.1	Ushigome 2015 (CHART 2)	10	6	Bonsu 2017	33.6	28.7
Senni 2014	18	14.1	Tsuji 2017	13.9	6	Shah 2017	21.7	16.4
Hamaguchi 2012	68	58	Farré 2017	5.5	5.3	-	-	-
Non CV mortality								
Chioncel 2017	1.8	1.9	Adabag 2012	8.6	10.9	Pascual-Figal 2017	6.6	10.7
Gomez-Otero 2017	4.6	3.9	Hamaguchi 2012	18	28	-	-	-
Senni 2014	3.7	4.2	Farré 2017	11.9	19.3	-	-	-

Data from longest follow up period was added from the studies reporting mortality at multiple time points

Table 3: Proportion of patients (%) with all cause mortality rates across HF phenotypes

Study name	HFrEF (%)	HFpEF (%)	Study name	HFrEF (%)	HFpEF (%)	Study name	HFrEF (%)	HFpEF (%)
Guisado-Espartero 2018	28	22	Nichols 2015	24	23	Pascual-Figal 2017	33	28
Wang 2018	16.5	15.4	Quiroz 2014	18.2	17.1	Kontogeorgos 2017	68.8	65
Chioncel 2017	8.8	6.3	Senni 2014	24.4	19.6	Gerber 2015	27.3	34.6
Gomez-Otero 2017	19.9	19.3	Lam 2018	19	14	Bermejo 2018	42.2	50.3
Koh 2017	15.4	17.4	Sanjay 2018	42.3	36.7	Bonsu 2017	34.5	30.1
Cheng 2014	37.5	35.6	Hai 2016	25.5	23.9	Shah 2017	75.3	75.7
Kapłon-Cieślicka 2016	21	17	Ather 2012	25.5	20	Caughey 2018	61	31
MacDonald 2016	17	15	Tsuji 2017	21.5	13.6	-	-	-
Hoong 2015	11.3	5.9	Farré 2017	45.8	52.6	-	-	-

Data from longest follow up period was added from the studies reporting mortality at multiple time points

CONCLUSION

- There was considerable variability in mortality estimates across different studies owing to baseline comorbidities, age of the patient population and sample size.
- In general, comparisons between HFrEF and HFpEF were broadly consistent with higher all cause, HF mortality, CV mortality and sudden death rates in HFrEF than in HFpEF. Non-CV mortality constituted a higher proportion of deaths in HFpEF than in HFrEF.
- Despite the higher contribution of non-CV mortality, the majority of deaths in HFpEF were still due to CV causes, reflecting a significant contribution of the disease to the overall mortality burden in this population.

References

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