Risk Stratification for Sudden Cardiac Death in Heart Failure

Hendry Purnasidha Bagaswoto

Department of Cardiology and Vascular Medicine, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada – Dr. Sardjito General Hospital, Yogyakarta, Indonesia

Corresponding author:
Hendry Purnasidha Bagaswoto, MD, - email: purnasidha_2002@yahoo.com
Department of Cardiology and Vascular Medicine, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada – Dr. Sardjito Hospital
Jalan Farmako Sekip Utara,Yogyakarta, Indonesia 55281

ABSTRACT

Heart failure (HF) is a complex clinical syndrome in which structural / functional myocardial abnormalities result in symptoms and signs of hypoperfusion and/or pulmonary or systemic congestion at rest or during exercise. More than 80% of deaths in patients with HF recognize a cardiovascular cause, with most being either sudden cardiac death (SCD) or death caused by progressive pump failure. Risk stratification of SCD in patients with HF represents a clinical challenge. This review will give an update of current strategies for SCD risk stratification in HF.

Introduction

Heart failure is a complex clinical syndrome with structural abnormality or a myocardial which resulted in signs and symptoms of hypoperfusion and/or pulmonary or systemic congestion during rest or activity.[1,2]

Sudden cardiac death is defined as death caused by unexpected stop in blood circulation that occurs within one hour from the start of symptoms or during sleep.[3] In the majority of cases, sudden cardiac death is triggered by arrythmia (e.g. ventricle tachycardia, ventricle fibrillation), although pulseless electrical activity (PEA) is recently reported as the cause of sudden cardiac death.[4]

Risk stratification for sudden cardiac death in heart failure patients with reduced ejection fraction still becomes a clinical challenge. Recent guideline provides an algorithm according to left ventricle ejection fraction in which this parameter is considered as the only parameter to identify high risk patients.[5] Nevertheless, current approaches cannot be used to stratify the population and risk spectrum with high accuracy.

Pathophysiology of Sudden Cardiac Death

The mechanism of sudden cardiac death in heart failure patients with reduced ejection fraction (HFrEF) is complex in nature and requires a chain of interaction between transient events with pathological basic substrate which triggers electric instability (Figure 1).

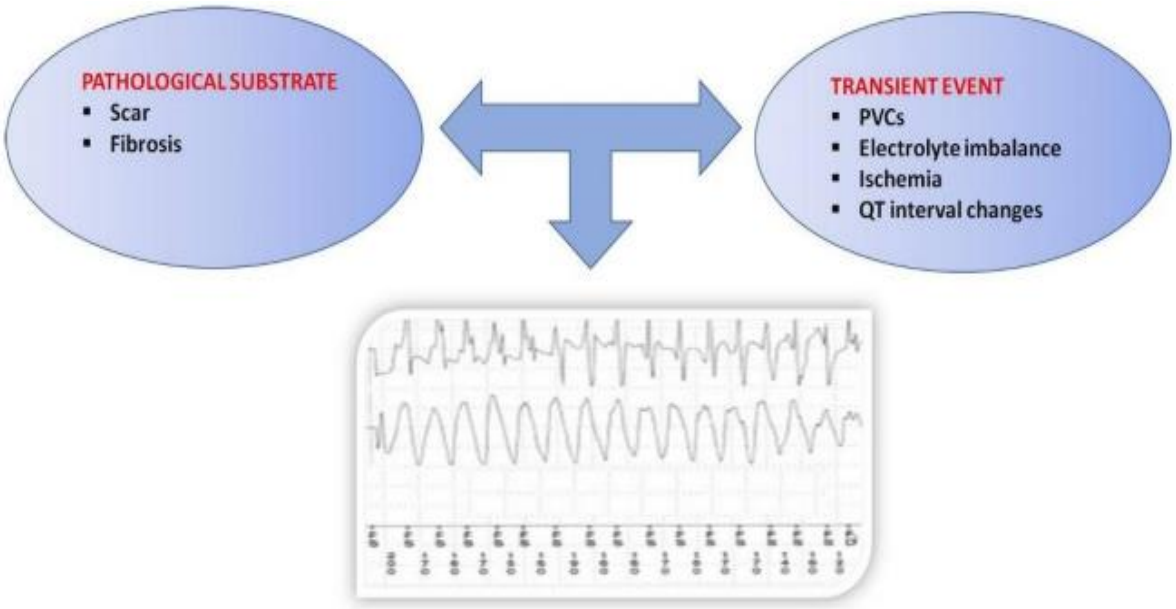

Figure 1. Anatomical substrate and pathophysiology of sudden cardiac death in heart failure with reduced ejection fraction. PVCs: premature ventricular complex; QT: QT interval[6]

In ischemic cardiomyopathy, sudden cardiac death is related to previously infarcted myocardial region near a thick scar that forms from time to time. Residual endomyocardial fiber can persist because the blood gives nutrition to this area in the ventricle (e.g. through retrograde perfusion through left atrial vein, retrograde perfusion through sinusoidal tract, or through oxygen diffusion from blood flow in ventricle through myocardium).[7] In patients with systolic dysfunction that occurs after myocardial infarction, sudden cardiac death caused by non-arrythmia often occurs within the first hour to six weeks and is related to a mechanical complication of myocardial infarction itself (e.g. rupture in the left ventricle wall, rupture in the interventricular septum and acute mitral regurgitation).[8]This showed that the proportion of sudden cardiac death caused by arrythmia and non-arrythmia to be the same after 1 month from myocardial infarction. This reason explains from the current guideline where implantable cardioverter defibrillator (ICD) is recommended in 40 days post myocardial infarction.[9,10] In non-ischemic cardiomyopathy, the ventricular myocardium has multiple fibrosis area without significant scar.[11] This finding explains why reentry only involves 40% of ventricular arrythmia mechanism in patients with non-ischemic cardiomyopathy, while the rest is caused by triggered activity process (for example early after depolarizations and delayed after depolarizations).[12,13]

The main mechanism of sudden cardiac arrest in heart failure patients with preserved ejection fraction (HFpEF) seems to be related to myocardial fibrosis which causes changes in regional conductive pattern and become the area of reentry.[14] Furthermore, ischemia is

thought to be a contributor that needs further investigation on ventricular arrythmia in HFpEF patients.[15] Without considering the cause of heart failure and the value of left ventricular ejection fraction, in patients with advanced heart failure, arrythmia is triggered primarily by heart pump failure where around 60% of patients had severe bradyarrhythmia or electromechanical dissociation as the primary cause of sudden cardiac death.[16]

Table 1. Sudden cardiac death risk factor in patients with HFrEF

Patient and Family History
- Previous Myocardial Infarction event
- Family history of sudden cardiac death
- Syncope without exact causes
Electrocardiography
- QRS complex duration
- T-wave alternans
- Signal averaged ECG
Autonomic function
- Heart rate variability
- Blood flow turbulence
Electrophysiology findings
- Easily triggered Ventricular arrhytmia
- Extensive low voltage / abnormal signals on electroanatomic mapping
- Broad scar area in mid-epicardium
- Multiple ventricular tachycardia morphology
Echocardiography findings
- Left Ventricle ejection fraction
- Ventricular disynchronized
- finding on speckle tracking
- Mechanical Dispertion
Cardiac MRI
- Late gadolinium enhancement
- T1 mapping
Myocardial Sympathetic Innervation Imaging
- Heart to mediastinal ratio
Biomarker
- Natriuretic peptide
- High sensitive troponin
- Soluble ST2
Genetic
- Lamin A/C Mutation
- Desmin Mutation

Risk Stratification of Sudden Cardiac Failure in HFrEF

Even though several risk factors on sudden cardiac death has been known and was thought to play a role in HFrEF (Table 1), risk stratification to determine which patient is beneficial to ICD placement as an effort of primary prevention to sudden cardiac death still arises a question.

Risk Stratification of Sudden Cardiac Death in HFpEF

In a recent study involving HFpEF population, sudden cardiac death is reported to be one of the most common cause of death. In CHARM (Candesartan in Heart Failure-Assessment of Reduction in Mortality and Morbidity) study, it was shown that sudden cardiac death is found in 28% of death.[17] Similar to this study, 26% of all cause of death in I-PRESERVE (Irbesartan in Patients with Hearth Failure and Preserved Ejection Fraction) study is related to sudden cardiac death.[18]

In daily clinical practice, risk evaluation to sudden cardiac death in patients with HFpEF specifically has still been a challenge, both from the variability of phenotype and high percentage of death due to non-cardiovascular. Table 2 described the risk factor in patients with HFpEF on sudden cardiac death.

Conclusion

Even though pharmacological and electrical therapy has advanced, sudden cardiac death is still the most common cause of mortality in patient with HFrEF. A pilot study has shown that left ventricle ejection fraction and ischemic process have been predictors to sudden cardiac death.

Nevertheless, epidemiological changes on sudden cardiac death require identification on risk stratification in the population. In regard to this, current imaging technique, ECG findings and genetic test can be used to improve the identification of individuals with high risk stratification which should be beneficial for specific approach to prevent sudden cardiac death (Figure 2).

On the other hand, patients with HFpEF also have high prevalence in sudden cardiac death. For this population, increasing the understanding of pathophysiological pattern of sudden cardiac death should improve risk stratification of sudden cardiac death.

Table 2. Sudden cardiac death risk factor in patients with HFpEF

History
- Age
- Male
- Diabetes Mellitus on insulin
- Previous Myocardial Infarction
Electrocardiography
- Left Bundle Branch Block
Biomarker
- Natriuretic Peptide

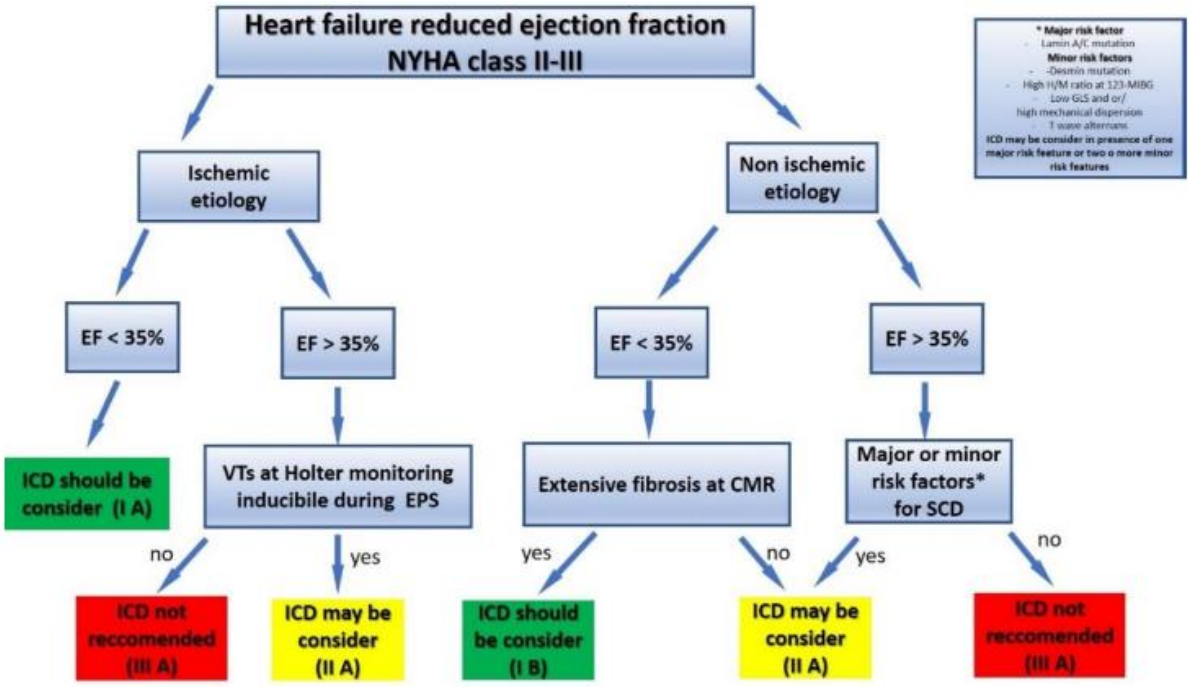

Figure 2. Risk stratification of sudden cardiac death in HFrEF patients
EF: Ejection fraction, VTs: Sustained ventricular tachycardias, ICD: Implantable cardioverter defibrillator, CMR: Cardiac magnetic resonance, H/M ratio: Heart/mediastinum ratio, GLS: Global longitudinal strain

References

1. Metra M., Teerlink J.R. 2017. Heart failure. Lancet, 390:1981–1995.
2. Masarone D., Limongelli G., Ammendola E., Verrengia M., Gravino R., Pacileo G. 2018. Risk stratification of sudden cardiac death in patient with heart failure: an update. J Clin Med, 7:436.
3. Al-Khatib S.M., Stevenson W.G., Ackerman M.J., Bryant W.J., Callans D.J., Curtis A.B., et al. 2017. 2017 AHA/ACC/HRS Guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: Executive Summary: A Report of The American College of Cardiology / American Heart Association Task Force on Clinical Practice Guidelines and The Heart Rhythm Society. J. Am Coll Cardiol, 1097:41305–413020.
4. Hayashi M., Shimizu W., Albert C.M. 2015. The spectrum of epidemiology underlying sudden cardiac death. Circ Res, 116:1887-1906.
5. Ponikowski P., Voors A.A., Anker S.D., Bueno H., Cleland J.G., Coats A.J., et al. 2016. 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 J Heart Fail, 18:891–975.

6. Masarone D., Limongelli G., Rubino M., Valente F., Vastarella R., Ammendola E., et al. 2017. Management of arrhythmias in heart failure. J Cardiovasc Dev Dis, 28:3.
7. Burke A.P., Virmani R. 2007. Pathophysiology of acute myocardial infarction. Med Clin N Am, 91:553–572.
8. Zaman S., Kovoor P. 2017. Sudden cardiac death early after myocardial infarction: pathogenesis, risk stratification and primary prevention. Circulation, 129:2426–2435.
9. Ibanez B., James S., Agewall S., Antunes M.J., Bucciarelli-Ducci C., Bueno H., et al. 2017. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for The management of acute myocardial infarction in patients presenting with ST-Segment elevation of the European Society of Cardiology (ESC). Eur Heart J, 39:119–177.
10. Priori S.G., Blomström-Lundqvist C., Mazzanti A., Blom N., Borggrefe M., Camm J., et al. 2015. 2015 ESC Guidelines for The management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The task force for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). Eur Heart J, 36:2793–2867.
11. Liuba I., Marchlinski F.E. 2014. The substrate and ablation of ventricular tachycardia in patients with non-ischemic cardiomyopathy. Circ J, 77: 1957–1966.
12. Pogwizd S.M., McKenzie J.P., Cain M.E. 1998. Mechanisms underlying spontaneous and induced ventricular arrhythmias in patients with idiopathic dilated cardiomyopathy. Circulation, 98:2404–2414.
13. Goldberger J.J., Subacius H., Patel T., Cunnane R., Kadish A.H. 2014. Sudden cardiac death risk stratification in patients with non-ischemic dilated cardiomyopathy. J. Am Coll Cardiol, 63:1879–1889.
14. Van der Bijl P., Delgado V., Bax J.J. 2017. Sudden cardiac death: the role of imaging. Int J Cardiol, 237:15–18.
15. Haugaa K.H., Goebel B., Dahlslett T., Meyer K., Jung C., Lauten A., 2012. Risk assessment of ventricular arrhythmias in patients with nonischemic dilated cardiomyopathy by strain echocardiography. J Am Soc Echocardiogr, 25:667–673.
16. Haugaa K.H., Smedsrud M.K., Steen T., Kongsgaard E., Loennechen J.P., Skjaerpe T., et al. 2010. Mechanical

dispersion assessed by myocardial strain in patients after myocardial infarction for risk prediction of ventricular arrhythmia. JACC Cardiovasc Imaging, 3:247–256.

17. Solomon S.D., Wang D., Finn P., Skali H., Zornoff L., McMurray J.J., et al. Effect of candesartan on cause-specific mortality in heart failure patients: the candesartan in heart failure assessment of reduction in mortality and morbidity (CHARM) program. Circulation, 12:2180–2183.
18. Zile M.R., Gaasch W.H., Anand I.S., Haass M., Little W.C., Miller A.B., et al. 2010. Mode of death in patients with heart failure and a preserved ejection fraction: results from the irbesartan in heart failure with preserved ejection fraction study (I-Preserve) Trial. Circulation, 30:1393–1405.