

## Frailty Syndrome: an Emerging Geriatric Syndrome Calling for Its Potential Intervention

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It is projected that the elderly population in Indonesia will increase from approximately 19 million people in 2010 with life expectancy of 69.8 years during period of 2005-2010 to 29 million people in 2020 (11.11% of total population) with life expectancy of 73.6 years during period of 2020-2025. Higher elderly female proportion compared to male (11.43% versus 10.78%) will also be found.<sup>1</sup> Aging process happens as people get older. Its process is influenced by genetic and environmental factors that can lead to successful aging, usual (normal) aging or pathologic aging. People with pathologic aging would have an increased risk to become frail.<sup>2,3</sup>

Nowadays, frailty syndrome is considered as one of the geriatric syndromes which increase the risk of worsening clinical outcome in mobility, functional status, hospitalization, institutionalization and mortality, as well as lower health-related quality of life.<sup>4,5</sup> Moreover, frailty syndrome reflects a biological age that predicts mortality risk better than chronological age [RR 1.57 (95% CI 1.41-1.74) versus RR 1.08 (95% CI 1.06-1.2)].<sup>6</sup> No wonder, frailty syndrome has attracted clinician's attention, especially the geriatricians, all over the world with increasing research in this field.

Frailty syndrome, a biological syndrome of decreased physiological reserved capacity and capability to endure upon stressors, can be perceived as a clinical syndrome (phenotype) or as deficits/co-morbidities/disabilities accumulation. Based on these two concepts, a

person can be classified as normal (fit/robust), pre-frail, and frail.<sup>6,7</sup>

As a phenotype, frailty syndrome is characterized by exhaustion due to poor endurance and lack of energy, as well as decrease in body weight (shrinking), muscle strength (weakness), gait speed (slowness), and physical activity. This concept of phenotype frailty differentiates frailty from disability.<sup>6</sup> In contrast, clinical approach of frailty syndrome as deficits accumulation takes into account disabilities in addition to co-morbidities as characteristics of frail people. This concept based on consideration that the more the deficits accumulated in a person, the frailer the person will be.<sup>7,8</sup>

There are numerous score systems to diagnose frailty syndrome, mostly derived from phenotype concept described by Fried et al.<sup>4</sup> in cardiovascular health study or deficits accumulation concept described by Rockwood et al.<sup>7</sup> in Canadian Study of Health and Aging. The prevalences of frailty syndrome differ one another depend on the score system or the clinical setting used in the study.<sup>8</sup> The concept of frailty syndrome is multidimensional to include physical, psychological and social domain, in which complex interactions among them contribute to the development and the severity of frailty syndrome.<sup>9</sup>

Gill et al.<sup>10</sup> shows the dynamic transition of frailty syndrome. It indicates that frailty syndrome is potentially reversible by managing modifiable contributing factors. Fried et al.<sup>4</sup> hypothesize the main element that contribute to physical frailty is sarcopenia (low of muscle

mass and function). Other conditions that may also contribute to development of frailty syndrome are inflammation, insulin resistance and diabetes mellitus (DM).<sup>11-13</sup>

Diabetes mellitus patients tend to have an accelerated aging process that increases the risk to become frail at younger age.<sup>14</sup> Insulin resistance has long been known to contribute to the development of type 2 DM. Longitudinal studies have shown that insulin resistance [HR 1.15 (95% CI 1.02-1.31) and hyperglycemia/A1C  $\geq$ 8% [HR 3.33 (95% CI 1.24-8.93)] raise the incidence of frailty syndrome.<sup>12,13</sup> Insulin resistance contributes to the increased inflammatory and pro-thrombotic state, endothelial dysfunction, atherosclerosis and changes in lipid metabolism. Insulin resistance has also been linked to sarcopenia with decreased gait speed and muscle strength.<sup>15</sup> Therefore, in this Acta Medica Indonesiana-The Indonesian Journal of Internal Medicine edition, we bring this topic of frailty in relation to therapy in type 2 DM elderly patients.

The oral anti-diabetic metformin is potentially able to modify factors contributing to frailty syndrome (insulin resistance, hyperglycemia, inflammation) through its activation on adenosine monophosphate-activated protein kinase (AMPK), while inhibiting mediator inflammation nuclear factor- $\kappa$ B (NF $\kappa$ B) and mammalian target of rapamycin (mTOR).<sup>16,17</sup> Moreover, animal studies show potential ability of metformin to delay aging process and prolong the animal's life span with various length of time depend on the species and strain.<sup>18</sup> Thus, the case-control study done by Sumantri et al.<sup>19</sup> to explore the relation between metformin use in elderly diabetics and the risk of frailty syndrome is important in providing insight about another beneficial effect of metformin. This study indicates that metformin has a protective effect against frailty syndrome in elderly patients with type 2 DM. Surely this result will provide direction for future research in frailty syndrome intervention.

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