

## The effect of body mass index (BMI) on the mortality among patients with stroke

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### **Abstract :**

*Stroke is considered one of the leading causes of morbidity and mortality in many countries. Many studies investigated the outcomes after the occurrence of stroke. Some of those research studies indicated that obesity and the increase in the body mass index are established risk factors for mortality among stroke patients. However, the results of these studies were inconsistent. The main aim of this review article was to examine the association between body mass index and mortality among stroke patients. The majority of the studies had shown a possible effect of overweight on mortality among stroke patients; the evidence regarding the association's presence is limited. On the other hand, the majority of the studies had shown a protective effect of obesity (mild obesity, body mass index between 30-35) on reducing the risk of mortality among stroke patients. This means underweight stroke patients have more risk of mortality. Thus, the argument regarding the effect of high body mass index on mortality has been explained by the obesity paradox. However, most of those studies were observational, and results could be attributed to the methodological flaw. There is a need to well-designed prospective studies that to overcome the limitation of the previous studies.*

**Keywords:** Body mass index, stroke, obesity, overweight, mortality

### **Introduction:**

Stroke is considered the fifth leading cause of death and a leading cause of morbidity and disability worldwide<sup>1</sup>. A stroke happens as result of the death of brain cells due to lack of oxygen supply caused by either a blocked artery by a clot (called ischemic stroke) or burst and rupture of blood vessels (called a hemorrhagic stroke)<sup>1</sup>. Many factors have been identified as risk factors for developing strokes, such as age, gender, cardiovascular risk factors, and lifestyle factors, including obesity and overweight<sup>2</sup>. Obesity is defined as having a body mass index (BMI) of 30.0 or more<sup>3</sup>. It is a significant public health problem and has been described as an essential risk factor for stroke. Thus, obesity is a risk factor for hypertension and diabetes, and those diseases also play a role in causing stroke through many mechanisms such as their impacting on a renin-angiotensin pathway and sympathetic nervous system<sup>4</sup>.

Many epidemiological studies had reported that obesity and overweight are strongly associated with increased risk of stroke, mainly ischemic stroke<sup>2</sup>. Currently, research had indicated that obesity is an established risk factor for mortality among stroke patients<sup>2,5,6</sup>. The results of these studies were inconsistent. Thus, some studies showed that obesity is associated with an increased risk of mortality among stroke patients, with most deaths occurring in the first month<sup>5</sup>. Other studies found a weak association between BMI and mortality among stroke patients<sup>7</sup>. Thus, some of the current evidence has been limited to the small size of their population, inability to control preexisting confounders such as cardiovascular disease and smoking<sup>8</sup>. Therefore this review article aimed to examine the association between BMI and mortality among stroke patients. The finding of this review will help us to identify if high BMI is considered a dependent risk factor for mortality, therefore, help clinicians to incorporate measures to reduce BMI among stroke patients.

### **Literature of review**

Stroke currently is considered the fifth leading cause of death and one of the most leading causes of morbidity and long-term disability worldwide<sup>1</sup>. In general, the prevalence of stroke has been increased in recent years due to the increasing aging population, changes in lifestyles, and the epidemic of diabetes<sup>9</sup>. Eight hundred thousand people each year experience a new or recurrent stroke<sup>10</sup>. A stroke happened when a clot or bursts blocked the blood vessel that carries oxygen and nutrients to the brain. When this occurs, some brain cells die because they don't have enough oxygen<sup>10</sup>.

There are two types of stroke. Ischemic stroke is the most common one. It happens when the brain arteries become narrowed or blocked, which causes a reduction in blood flow (ischemia). Ischemic strokes; therefore, occurs by either a clot (thrombus) that forms in one of the arteries that supply blood to the brain (in this case, it is called Thrombotic stroke) or a blood clot that happens away from the brain and goes through the bloodstream to lodge in narrowing the brain arteries (in this case it called Embolic stroke)<sup>9,11</sup>. The second type of stroke is hemorrhagic stroke, and it happens when a blood vessel of the brain leaks or ruptures. Hypertension, a blood thinner, and aneurysms are all causes of hemorrhagic stroke<sup>11</sup>.

Many factors have been identified as risk factors for developing strokes, such as age, gender, cardiovascular risk factors, and lifestyle factors, including obesity and overweight<sup>2</sup>. Obesity is defined as having a body mass index (BMI) of 30.0 or more<sup>3</sup>. A recent meta-analysis found that the effect of BMI on stroke is mediated by blood pressure, glucose level, and cholesterol level<sup>12</sup>. Therefore, obesity considers an important public health problem and has been defined as an essential and preventable risk factor for stroke.

A total of 12 studies have been identified in this literature review through searching on the PubMed database. We used the following words in the searching process: Obesity, BMI, overweight, underweight, stroke, and mortality in the title or the abstract. Many studies had identified obesity as a risk factor for stroke<sup>2</sup>. However, the available evidence regarding the increase in the risk factor of BMI and obesity on the

mortality among stroke patients stills controversial. Thus some of the studies have reported an increase in the risks while others showed no association. Therefore, considerable uncertainty remains about this topic.

In this review, we discussed the evidence related to the effect of increasing the BMI on the mortality after stroke in which we divided the evidence into those who support the presence of an association between high BMI and mortality after stroke and to those who reported that there isn't an association between BMI and mortality among stroke patients.

**Evidence that supports the effect of body mass index on the mortality among stroke patients:**

There are some studies found that there is an increase in mortality among stroke patients who have high BMI. For instance, in 2001, a group of researchers conducted a cohort study in which they followed up stroke patients to determine the overall mortality among this cohort study<sup>13</sup>. They found that BMI was an independent risk factor associated with increasing the incidence of mortality among stroke patients<sup>13</sup>. This study was followed by a cross-sectional study of a national survey in the United States (US) to assess the association between BMI and mortality<sup>5</sup>. They reported an association between an increase of all-causes of mortality and increased BMI spicily in the younger population<sup>5</sup>. This evidence had triggered more researchers to quantify the association between the increase of BMI and mortality. Thus, a pooled data from 97 cohort studies revealed that the hazard ratio for stroke was 1/18 (95% confidence Interval CI 1.14-1.22) for BMI of (5kg/m<sup>2</sup>) increase in the BMI<sup>12</sup>.

Some of the studies examined obesity and elevated BMI on mortality among patients with acute ischemic stroke<sup>14</sup>. That study showed that patients with an acute ischemic stroke with lower and higher BMI had increased mortality<sup>14</sup>. A recent study in 2017 reported that BMI increase in adolescence is associated with the risk of stroke, contributing to the rise in the observed association between stroke and mortality. The postulated biological mechanism for this association suggested that obesity indirectly has cardiovascular and metabolic effects following the episodes of stroke<sup>15</sup>.

**Evidence that doesn't support the effect of body mass index on the mortality among stroke patients:**

In contrast, a number of research studies had shown that stroke patients who have high BMI might have protective or have no association with mortality. The mechanism of this had been described as the phenomenon of the "obesity paradox"<sup>16-18</sup>. Thus the obesity paradox attributed to the idea of protective effect of fat in patients with fragile metabolic status<sup>18</sup>. This phenomenon has been examined in all-cause of mortality among patients with cardiovascular disease. Also, it has been investigated in patients with stroke<sup>16-18</sup>. Thus, these studies had indicated that increasing BMI had an inverse association with all-causes of mortality among stroke patients<sup>18</sup>. In 2008, Olsen et al. followed stroke patients for five years, and they reported that the risk of mortality was lower among overweight patients than stroke patients who had average body weight (Hazard Ratio HR of 0.73 95%CI 0.74-0.96)<sup>19</sup>. Also, many studies had reported a

protective effect of obesity at certain ages with a U shape relationship between BMI and mortality<sup>14,15</sup>. This phenomenon, therefore, indicated that the effect of obesity on allcauses of mortality is mainly age-dependent<sup>20</sup>.

Thus, higher mortality risk was observed among stroke patients with lower or higher BMI. Whereas those who have BMI of approximately 35kg/m<sup>2</sup> had the lowest mortality<sup>14</sup>. This trend also has been investigated in which the investigator examined the stroke outcome among patients with atrial fibrillation (AF) treated with anticoagulant therapy<sup>21</sup>. Although that study has reported a possible protective effect of the anticoagulant therapy in reducing the mortality post-stroke, they also noted that increased BMI was associated with decreased risk of stroke and the associated mortality<sup>21</sup>.

The contradictory evidence regarding the effect of BMI on mortality after a stroke had promoted a group of researchers to conduct a systematic review and meta-analysis of the protective effect of BMI on total mortality<sup>20</sup>. That study illustrated that obese stroke patients had an 83% reduction in the risk of mortality after stroke compared to underweight patients<sup>20</sup>. Many studies had reported the protective effect of increase in body weight on the mortality after stroke especially among patients with ischemic stroke<sup>6,22</sup>. Finally, a recent nested case control study in 2017 showed that patients with BMI  $\geq 25$  had better 10 years survival after ischemic stroke compared to stroke patients with BMI between 18-25<sup>15</sup>.

In addition, a number of studies had indicated the absence of the effect of increasing BMI on the risk of mortality among patients who had stroke<sup>6,23</sup>. Sun et al, reported in their study that there were no association between increase in obesity with mortality<sup>6</sup>. Also, a study examined the short term mortality after the stroke and conclude that after 3 months of follow up there were no significant difference in mortality between overweight and underweight<sup>23</sup>.

### Conclusion:

In summary, the majority of observational studies reported a decreased mortality rate in overweight patients, and this association remained statistically significant even after the adjustment of confounder. Many methodological flaws were noted in the abovementioned observational studies that limit the ability to confirm the protective effect of BMI on mortality. Further studies that overcome these limitations would be the best recommendations from this review. Clinicians should provide advice and the appropriate management plan to stroke patients to reduce the morbidity and mortality of stroke.

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