

## Cardiovascular Risks Associated With Obesity in Children and Adolescents

Ting Fei Ho,<sup>1</sup>MBBS, MD, FRCP (Edin)

### Abstract

**Introduction:** The aim of this paper is to review the cardiovascular (CVS) risks associated with obesity in children and adolescents. Both short-term and long-term CVS consequences, the mechanisms of how these develop and the measures that can alter or reverse these CVS events are reviewed. **Materials and Methods:** Selected publications include original articles and review papers that report on studies of CVS risks and consequences related to childhood obesity. Some papers that contain data from adults studies are also included if the contents help to explain some underlying mechanisms or illustrate the continuation of related CVS changes into adulthood. **Results:** Obese children and adolescents have an increased risk for CVS complications that include elevation of blood pressure, clustering of CVS risk factors (Metabolic Syndrome), changes to arterial wall thickness, elasticity and endothelium, as well as changes in left ventricular structure and function. Some of these cardiovascular problems may be initiated or potentiated by obstructive sleep apnoea that can accompany obesity in children. Many of such changes have been noted to reverse or improve with weight reduction. **Conclusions:** Early development of CVS risks in obese children and the possible continuation of CVS complications into adulthood have been observed. Obstructive sleep apnoea in obese children can further contribute to such CVS risks. These findings underscore the importance of prevention of childhood obesity as a priority over management of obesity in children.

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**Key words:** Endothelial function, Hypertension, Metabolic syndrome, Obstructive sleep apnoea

### Background

#### *Adult Obesity and Cardiovascular Disease*

The prevalence of obesity has risen by three-folds or more in many countries since 1980. In 2005, it was estimated that globally there are about 1.6 billion overweight adults and at least 400 million of them are obese.<sup>1</sup> This increase in the prevalence of adults being overweight and obese comes with a heavy price. The cost of healthcare has significantly increased and is expected to increase even more because of the close association between obesity and various chronic diseases.

The association of obesity with chronic diseases in adults, in particular cardiovascular diseases, is well known.<sup>2</sup> One of the most important cardiovascular diseases associated with obesity is hypertension. Risk estimates from population studies suggest that more than 75% of hypertension can be directly attributed to obesity.<sup>3</sup> Increase in blood pressure in obese adults can contribute to left ventricular hypertrophy.<sup>4</sup> However, abnormal left ventricular mass and function can occur in obese adults in

the absence of hypertension<sup>5</sup> and can be related to the severity of obesity.<sup>6</sup>

Increasing weight also has a strong correlation with the elevation of triglyceride and low-density lipoprotein (LDL) cholesterol levels as well as low high-density lipoprotein (HDL) levels. Furthermore, the increase in body fat is positively linked to metabolic disorders of which insulin resistance is one of the key changes. The Metabolic Syndrome (MS) represents a clustering of metabolic abnormalities that are risk factors for cardiovascular disease. These metabolic abnormalities include insulin resistance, impaired glucose tolerance, type II diabetes, dyslipidaemia and increased blood pressure, as defined by the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III).<sup>7</sup> Adult patients with MS have an increased risk of coronary heart disease and stroke,<sup>8-12</sup> while MS and abdominal obesity have been found to be associated with endothelial dysfunction.<sup>13-16</sup> Some studies have indicated that obesity independently predicts coronary atherosclerosis in both men and women.<sup>17-19</sup> Middle age

<sup>1</sup> Department of Physiology, Yong Loo Lin School of Medicine, National University of Singapore

Address for Correspondence: Dr Ho Ting Fei, Department of Physiology, Yong Loo Lin School of Medicine, National University of Singapore, Block MD 9, 2 Medical Drive, Singapore 117597.

Email: phshotf@nus.edu.sg

men and women with increased BMI have an increased risk of non-fatal or fatal coronary heart disease.<sup>19,20</sup>

### Childhood Obesity and Cardiovascular Disease

The prevalence of being overweight and obese in children and adolescents is also increasing rapidly both in high income as well as middle and low-income countries. There are about 155 million overweight children worldwide, of which about 30 to 45 million are obese.<sup>21</sup> Throughout the world, children are becoming overweight and obese at progressively younger ages.<sup>1</sup>

It was earlier thought that obese children do not develop cardiovascular problems until they reach adulthood. However, it is now recognised that obese children can have short-term and long-term cardiovascular complications. Blood pressure (BP) was found to increase with body mass index (BMI) in children.<sup>22</sup> Obese children who have high BP were at increased risks of left ventricular hypertrophy.<sup>23</sup> Weiss et al reported that the prevalence of MS increased with the severity of obesity and as high as 50% of the severely obese children and adolescents had MS.<sup>24</sup> In the Bogalusa study where young adults were tracked from childhood for 22 years, childhood LDL cholesterol level and childhood BMI were found to be predictors of carotid intima-media thickness (IMT) in adulthood.<sup>25</sup> In another study where cardiovascular risk factors were measured in a group of young adults when they were 3 to 18 years of age, LDL cholesterol, systolic BP and BMI were associated with adult carotid IMT after adjusting for age and sex.<sup>26</sup> These studies serve to warn us that cardiovascular disease begins in childhood and is associated with risk factors such as BP, obesity, elevated cholesterol levels and diabetes that are present since childhood.

The objective of this paper was to review the information relating to the short-term and long-term cardiovascular risks in obese children and adolescents. Examples from adult studies will be included primarily for the purpose of comparison or to emphasise certain points, particularly when data from paediatric studies are lacking.

### Cardiovascular Diseases Associated With Childhood Obesity

Obesity in children and adolescents increases the risk for various cardiovascular problems (Table 1). Increase in body mass index is often an independent risk factor for the development of elevated blood pressure, clustering of various cardiovascular risk factors in metabolic syndrome, abnormal vascular wall thickness, endothelial dysfunction and left ventricular hypertrophy. The close link between obesity and obstructive sleep apnoea (OSA) has also raised the concern that many of these cardiovascular changes observed in obesity may be partially initiated by or linked to the presence of OSA.

Table 1. Cardiovascular Risks Associated with Obesity in Children and Adolescents

Cardiovascular/Metabolic Factor	Risks/Consequences
Blood pressure	Elevation of blood pressure / hypertension
Systemic arteries	<ul style="list-style-type: none"> <li>• Endothelial dysfunction</li> <li>• Increased carotid artery stiffness</li> <li>• Increased carotid artery intima-media thickness</li> </ul>
Left ventricle structure/geometry	<ul style="list-style-type: none"> <li>• Increased left ventricular mass / left ventricular hypertrophy</li> <li>• Increased left ventricular diameter</li> </ul>
Metabolic syndrome	Clustering of cardiovascular risk factors (obesity, elevated blood pressure, insulin resistance, dyslipidaemia)

### Blood Pressure

#### *BMI and Blood Pressure*

Longitudinal data from the Muscatine Study in children between 7 and 18 years of age show that adult BP is correlated with childhood BP and body size.<sup>27</sup> Several studies in the 1970s and 1980s documented the association between obesity and the elevation of BP in children.<sup>28-32</sup> It was noted that obesity was the most important factor affecting BP distribution in children.<sup>28-31,33-34</sup> Obese children have been found to have higher BP than normal weight children<sup>35</sup> and even for normotensive obese children, obesity is a risk factor for the future development of hypertension.<sup>36</sup> More recently, a study of school children between 8 and 13 years of age revealed that the prevalence of elevated BP was higher among overweight Hispanic children.<sup>34</sup> The overweight/obese children were 3 times as likely to present with high BP, after adjusting for confounding factors. In a case-control study of younger children of preschool age (0.1 to 6.9 years) in China, 19.4% of the children in the obese group had BP value (either systolic BP or diastolic BP) above the 95<sup>th</sup> percentile value as contrast to 7.0% in the non-obese group.<sup>37</sup> Both systolic and diastolic blood pressures were positively correlated with BMI. Assessing the longitudinal trends of BP in a group of children categorised as normotensive, pre-hypertensive and hypertensive in the Bogalusa Heart Study, Srinivasan et al found that pre-hypertensive and hypertensive children had significantly higher BP and BMI compared to the normotensive group. Such trends prevailed from childhood through adolescence.<sup>38</sup> Chioloro et al observed that in a rapidly developing country such as the Seychelles, both systolic and diastolic BP were strongly associated with BMI in boys and girls between the ages of 5 and 16 years.<sup>39</sup> Increasing proportions of children with elevated BP were found among those with normal weight (7.5%), overweight (16.9%) and obese (25.2%).

### *Consequences of Elevated Blood Pressure*

The cardiovascular consequences of the elevation of BP in young children have not been well documented. However, the early impact of pre-hypertension and hypertension on cardiac and systemic haemodynamic parameters in adolescents and young adults were examined in the Strong Heart Study.<sup>40</sup> Compared with normotensive individuals (53%), both pre-hypertensive (65%) and hypertensive (75%) individuals were more likely to be obese. Seventy nine percent of the hypertensive and 69% of the pre-hypertensive individuals had central adiposity as determined by waist circumference. The pre-hypertensive and hypertensive individuals had higher heart rate and cardiac output whether in absolute values or after adjustment for age, gender and other covariates. These individuals also had thicker interventricular septum and left ventricular posterior walls than normotensive individuals and their left ventricular chamber diameter and relative wall thickness were also increased. Thus left ventricular mass was greater and the prevalence of left ventricular hypertrophy was more than 3-fold higher in the hypertensives and 2-fold higher in the pre-hypertensives when compared to the normotensive individuals.

### *Mechanisms Contributing to Elevation of Blood Pressure in Obesity*

The mechanisms contributing to the development of hypertension in obese children are not well established. It has been suggested that renal sodium and water retention<sup>41</sup> and increased activation of the sympathetic and renin-angiotensin systems<sup>42,43</sup> may be responsible for the elevation of BP. Obesity is known to be associated with salt retention and increased cardiac output.<sup>44</sup> Such events would be expected to produce elevated natriuretic peptide levels. More recently, however, it has been observed that low circulating natriuretic peptide levels may contribute to the elevation of BP.<sup>45</sup> It is postulated that the low natriuretic levels may be due to an abundance of natriuretic peptide clearance receptors (NPR-C) in adipose tissue. Secondly, reduced secretion of natriuretic peptides may arise from decreased myocardial hormone release<sup>46</sup> or impaired synthesis.<sup>47</sup> Pausova et al shed some light on the genetic background of obesity-related hypertension. The study of 389 individuals from 55 extended families allowed a genome-wide scanning of the entire group. The data revealed that in the sub-set of families with obesity-related hypertension, the most significant locus was found in chromosome one in the region (D1S1597).<sup>48</sup>

### *Effect of Weight Loss on Blood Pressure*

Many studies regarding the effects of weight loss on hypertension suffer from deficiencies like small sample sizes and short-term follow-up. Aucott et al created a

model of the long-term effects of weight loss on BP.<sup>49</sup> It was revealed that, with the exception of surgical weight loss where changes in BP were insignificant, each kilogram of weight loss resulted in a decrease in systolic and diastolic BP of 4.6 and 6.0 mmHg, respectively. Such decrease was significantly greater than what was found in most other studies with short-term follow-up where each kilogram of weight loss only produced a 1 mmHg overall drop in BP.

## **Clustering of Cardiovascular Risk Factors**

### *BMI and Clustering of Cardiovascular Risk Factors*

The occurrence of elevated BP in obese children may not occur alone. Obese children and adolescents have been found to have abnormal levels of blood pressure, lipids and insulin.<sup>50-53</sup> Such clustering of cardiovascular risk factors is increasingly seen as the global prevalence of obesity in children increases. In the Bogalusa Heart Study, more than 9000 children between 5 and 17 years old were screened. Eleven percent of them were overweight, as defined by a Quetelet index  $\geq 95^{\text{th}}$  percentile value. The odds ratio for having various risk factors like elevated BP, abnormal lipids and insulin ranged from 2.4 (diastolic BP) to 12.6 (insulin).<sup>54</sup> In the National Heart, Lung and Blood Institute Growth and Health Study (NGHS), girls between 9 and 10 years old to 18 years old were followed longitudinally to young adulthood (21 to 23 years old).<sup>55</sup> Those who were overweight (defined using age-specific 95<sup>th</sup> percentile BMI values for girls) during childhood were 11 to 30 times more likely to be obese when they become young adults. Unhealthy systolic and diastolic BP, high-density lipoprotein (HDL) cholesterol and triglyceride levels were already present in overweight girls as young as 9 years of age. In a group of 10 to 15 year old black and white boys, overweight boys were found to have lower HDL cholesterol, higher LDL cholesterol and triglyceride levels, and higher systolic and diastolic BP than non-overweight boys.<sup>56</sup> Central obesity, as measured by the sum of truncal skinfold thicknesses, was associated with increased clustering of risk factors in overweight boys.

### *Cardiovascular Consequences of MS in Obese Children*

In more recent years, MS is not only recognised in obese adults but also in obese children.<sup>24,57</sup> The occurrence of such clustering of cardiovascular risk factors may explain the increased risk of adult coronary heart disease. Baker et al investigated the association between BMI in childhood (7 to 13 years of age) and coronary heart disease in adulthood (25 years or older) in a huge cohort of men and women in whom childhood BMI data was available.<sup>58</sup> The risk of either a non-fatal or fatal cardiovascular event was positively associated with BMI at 7 to 13 years old for boys and 10 to 13 years old for girls. Children with higher BMI were at an increased risk for coronary heart disease in

adulthood and the associations were linear for each age. Using a coronary heart disease risk modelling programme, Bibbins-Domingo et al computed that at the current rate of adolescent obesity in the United States, the prevalence of coronary heart disease will increase by a range of 5% to 16% by 2035.<sup>59</sup> More than 100,000 excess cases of coronary heart disease can be attributed to the increased obesity burden.

## Vascular Structure and Function

### *Endothelial Function*

Endothelial dysfunction is one of the early features of arterial atherosclerosis.<sup>60</sup> Such changes are known to commence in childhood<sup>61,62</sup> and are present in severely obese children.<sup>62</sup> Woo et al assessed arterial endothelial function by measuring endothelial-dependent dilation of the brachial artery in a relatively small group of mild to moderately obese children as versus non-obese children.<sup>63</sup> Brachial artery endothelial function was impaired in the obese children who were otherwise healthy and the degree of endothelial dysfunction was correlated with BMI.

### *Effect of Diet and Exercise on Endothelial Function*

In a study of whether obesity-related arterial dysfunction is reversible by diet and/or exercise in children, Woo et al noted that brachial artery endothelial function was initially impaired in overweight children. However, improvement in endothelial function was observed in these children after 6 weeks of diet modification only or a combination of diet and exercise programme.<sup>64</sup> A combination of diet and exercise led to the better improvement of endothelial function as contrast to diet alone. Vascular function was significantly better in children who persisted with the exercise programme as contrast to those who withdrew from the exercise programme. This study demonstrated the benefits of diet and exercise on endothelial function. Furthermore, it also highlighted the importance of a continued programme of exercise in helping to sustain the improvements on endothelial function.

### *Mechanism of Endothelial Dysfunction*

Endothelial dysfunction is an early process in the development of atherosclerosis. It is believed to be largely due to an impairment in the bioavailability of nitric oxide (NO) which is a vasodilator and also inhibits monocyte adhesion, platelet aggregation and smooth muscle proliferation.<sup>60,65</sup> Some have postulated this may be an insulin-mediated impairment of NO release.<sup>66</sup> It can also be due to a suppression of adipocyte lipolysis and elevated free fatty acid levels seen in those with abdominal obesity.<sup>67</sup> In the absence of the above factors, the most plausible explanation for endothelial dysfunction may be directly

linked to the secretory products of adipocytes in individuals with abdominal obesity. Adipocytes are known to secrete various peptide hormones and cytokines. Some of these are known to be able to alter vascular function.<sup>68</sup> High levels of adipocyte-derived angiotensinogen can enhance the local arterial renin-angiotensin system thus giving rise to excessive vascular tissue production of superoxide.<sup>69,70</sup>

### *Factors Influencing Carotid Artery IMT and Elasticity*

Coronary artery disease is a possible cardiovascular event associated with obesity in adults. However, as mentioned above, early features of arterial atherosclerosis can begin in childhood. Advancement of ultrasonographic techniques allows non-invasive and reliable detection of carotid IMT as a strong surrogate of coronary atherosclerosis.<sup>71</sup> Additional measurements of carotid arteries provide information on the functional properties of the arteries such as arterial elasticity and stiffness.<sup>72-74</sup> While arterial elasticity can be influenced by various physiological factors, cardiovascular risk factors associated with insulin resistance are important considerations.<sup>75,76</sup>

In a small group of mild to moderately obese but otherwise healthy children, Woo et al noted that obesity was associated with increased carotid IMT.<sup>63</sup> This highlights the fact that carotid stiffness and increased IMT do not occur just in severely obese children<sup>62</sup> but also in less obese children where the obesity is not confounded by other coexisting cardiovascular risk factors. In the Bogalusa Heart Study, multivariate analysis revealed that blood pressure, product of heart rate and pulse pressure, triglycerides, BMI and male gender were independent correlates of carotid artery elasticity in asymptomatic young adults.<sup>77</sup> Childhood measures of LDL cholesterol and BMI were significant predictors of carotid IMT in young adults.<sup>25</sup> While the association between MS and carotid IMT and stiffness has not been investigated in children, data from the Baltimore Longitudinal Study on Aging revealed that MS was an independent determinant of carotid IMT and stiffness in adults.<sup>78</sup> This association cannot be ruled out considering that atherosclerosis and MS have been detected in young obese children.

While increased carotid IMT and stiffness may be observed in obese children, studies have documented that weight loss can lead to improvement in the vascular properties. Rainer et al reported that in a cohort of 56 pre-pubertal obese children, those who had substantial weight loss after a 1-year outpatient intervention programme were found to have significantly improved carotid IMT, blood pressure, triglycerides, insulin and insulin resistance index.<sup>79</sup> Similarly, Woo et al reported that a programme of diet and/or exercise was able to reverse the increased carotid IMT and brachial endothelial function present in mild to

moderately obese children 9 to 12 years of age.<sup>64</sup>

#### *Mechanisms of Increased Carotid Artery IMT and Stiffness*

The mechanism of how carotid artery thickness and stiffness can increase in obese children is still uncertain. Arterial wall structure and function are influenced by and can be remodelled by changes in circumferential wall stress and flow-mediated shear stress of which blood pressure and blood flow are important determinants.<sup>80-84</sup> Impaired elasticity of larger arteries has been found to be an antecedent factor in the development of hypertension.<sup>74,85</sup> Furthermore, Urbina et al has observed an independent positive association between carotid stiffness and the product of heart rate and pulse pressure.<sup>77</sup> A hyperdynamic circulation is manifested by a widened pulse pressure and tachycardia. Insulin resistance syndrome is a condition that can contribute to such hyperdynamic state.<sup>86</sup> A hyperdynamic circulation can lead to repetitive cycles of stress and strain on the arteries and can thus contribute towards the development of arterial wall stiffness. It was demonstrated that *in vitro* cyclic stretching of the arterial wall can increase smooth muscle cell growth and synthesis of matrix components thus influencing arterial stiffness.<sup>87,88</sup> Therefore, one can hypothesise that, given the existence of various cardiovascular risk factors including elevated blood pressure and insulin resistance in obese children, progressive remodelling of the arterial wall leading to arterial wall thickening and increasing stiffness can occur from an early age.

#### **Left Ventricular Geometry and Function**

##### *Factors Affecting Left Ventricular Geometry and Function in Obesity*

Obesity is known to be an independent risk for coronary artery disease, ventricular dysfunction, congestive heart failure and cardiac arrhythmias in adults.<sup>2</sup> Increased left ventricular mass, systolic and diastolic hypertension have been found in obese adults.<sup>5,89,90</sup> In a cohort of young adults in the CARDIA Study, increasing BMI and systolic blood pressure over a 10-year interval was strongly related to left ventricular mass (LVM) in Black men and women as well as White women.<sup>91</sup> Daniels et al reported the findings of increased LVM in overweight children and adolescents.<sup>92</sup> This is strongly associated with an increased systolic blood pressure and lean body mass, suggesting that left ventricular hypertrophy (LVH) may be a compensatory response to increased cardiac workload. In fact, 82% to 86% of variability of LVM may be explained by phenotypic variations in body size and cardiac workload.<sup>93</sup> In both Black and White children and young adults in the Bogalusa Study, there was a significant association between the degree of obesity and LVM.<sup>94</sup> Furthermore, obesity in

childhood significantly predicts LVM in adulthood.

Nevertheless, other studies have reported increased prevalence of LVH in obese children or adolescents with or without hypertension.<sup>23,95</sup> In the Strong Heart Study, overweight and obese adolescents were found to have greater LV diameter and mass.<sup>96</sup> In the overweight adolescents, increased levels of LVM are appropriate to compensate for the higher haemodynamic load. However, in obese adolescents, the increase in LVM exceeds the need to compensate for increased haemodynamic load. In fact, in these obese adolescents, increase in LVM is associated with mildly reduced LV myocardial performance. These findings suggest that there are other non-haemodynamic factors that can contribute to the inappropriate increase in LVM in obese adolescents. A possible reason is the contribution of neurohumoral factors arising from the clustering of metabolic factors since the prevalence of MS was high in these obese adolescents.<sup>96</sup> Increasing insulin resistance may play a critical role in the development of myocardial hypertrophy.<sup>97</sup> The powerful protein-anabolic effect of insulin and its multiple functions beyond glucose control give insulin an important role in the pathogenesis of cardiomyopathy and heart failure syndrome.<sup>98-100</sup>

##### *Association between Arterial IMT and Left Ventricular Mass*

The relationship between carotid artery IMT and LVM was investigated in a group of children with elevated blood pressure. LVM was indexed to height to give the LVM index. Children with increased carotid IMT had higher LVM index compared to those with normal carotid IMT. Prevalence of LV hypertrophy was 89% in those with increased carotid IMT in contrast to 22% in those with normal carotid IMT.<sup>101</sup> Carotid IMT was positively correlated with BMI and LVM index. This study demonstrates that early arterial wall changes and LV hypertrophy can occur in parallel as evidenced by the high percentage of LV hypertrophy in children with increased carotid IMT. While there was an independent relationship between carotid IMT and LVM index after controlling for BMI, other atherogenic factors often associated with obesity were not assessed in this study. It is worthwhile noting that neither carotid IMT nor LVM index had any correlation with clinic blood pressure.<sup>101</sup> Although clinical symptoms may not appear in such children until many years later, these evidence are strongly suggestive that the atherogenic process can start early in childhood. Gatzka et al had earlier shown that aortic stiffness was higher in adults with coronary artery disease as compared to healthy controls.<sup>102</sup> In addition, LVM index was also higher in those patients with coronary artery disease. However, mean arterial blood pressure was identical in the patients with coronary artery disease and the healthy controls although pulse pressure was

significantly higher in those with coronary artery disease. This indicates that subjects with coronary artery disease had significantly stiffer proximal aortas and the higher LVM index might reflect the effect of higher output impedance associated with increased aortic stiffness or a higher cardiac load.<sup>102</sup>

#### *Obstructive Sleep Apnoea (OSA) and the Risk of Cardiovascular Disease in Childhood Obesity*

Being overweight and obese are known to be significant risk factors for OSA in adults as well as children.<sup>103-107</sup> While it is recognised that obesity increases the risk for cardiovascular abnormalities, it has been suggested that some of the cardiovascular consequences of obesity may be initiated or contributed by OSA. It has thus been proposed that there may be OSA-dependant and OSA-independent pathways in the development of cardiovascular diseases related to obesity.<sup>108</sup> The increasing prevalence of obesity in children is accompanied by an increase in the incidence of children and adolescents presenting with OSA where the severity of OSA is observed to be proportional to the degree of obesity.<sup>105-107</sup>

The occurrence of OSA can lead to morbidity affecting various target organs of which cardiovascular morbidity is an important consideration even in children (Table 2).<sup>109</sup> OSA can contribute to various cardiovascular consequences in association with obesity through multiple interacting pathophysiologic mechanisms.<sup>108-110</sup> Recurrent episodes of partial or complete upper airway obstruction during sleep resulting in hypoxia and hypercapnoea can lead to various neurohumoral changes, oxidative stress, inflammatory response and metabolic dysfunction.

#### *Mechanisms Underlying Cardiovascular Morbidity in OSA*

Various cardiovascular abnormalities have been observed in children with OSA. Altered regulation of blood pressure<sup>111</sup> and increased systemic blood pressure has been reported in

children with OSA.<sup>112,113</sup> These changes may perhaps be attributed partially to an increased activation of the sympathetic system<sup>114,115</sup> and endothelial dysfunction.<sup>116</sup> The latter is likely to be due to inflammatory responses in the blood vessels as a consequence to the release of inflammatory markers like C reactive protein and other vasoactive substances like endothelin-1.<sup>110,117</sup> Such changes may occur independently of obesity. Other mechanisms have been suggested that may mediate the association of OSA with hypertension. These are impaired arterial baroreflex activity, altered renal function, hyperleptinaemia, insulin resistance, activation of renin-angiotensin system and oxidative stress.<sup>118</sup>

While some studies in adults have indicated OSA to be a risk factor for the development of MS<sup>119-120</sup> a couple of studies have shown conflicting results suggesting that there is probably little or no association between OSA, obesity and MS in children.<sup>121-123</sup>

Several adult studies have investigated the relation between OSA and other cardiovascular changes. These have not been well substantiated in obese children. Some of these conditions include atherosclerosis which is thought to be initiated by endothelial damage and ongoing inflammatory response.<sup>108,124</sup> In OSA, frequent episodes of hypoxia can be a mechanism that induces repetitive pulmonary vasoconstriction eventually leading to pulmonary hypertension.<sup>109,125,126</sup> The above cardiovascular events have not been well documented in obese children with OSA but remain possibilities that deserve careful investigation.

#### **Conclusion**

There is increasing evidence to indicate that obesity in children and adolescents is associated with short- and long-term cardiovascular risks that include haemodynamic changes, structural and functional changes in the heart and blood vessels. Many of these are interrelated and some are

Table 2. Cardiovascular Morbidity Associated with Obstructive Sleep Apnoea in Obese Children

<b>Known cardiovascular morbidity associated with OSA as observed in obese children</b>	<b>*Possible long-term cardiovascular morbidity associated with OSA (inadequate evidence in obese children)</b>
Altered regulation of blood pressure	Atherosclerosis; abnormal structural and functional properties of large arteries
Elevated blood pressure	Pulmonary hypertension; <i>cor pulmonale</i>
Altered cardiac geometry	Abnormal ventricular systolic or diastolic function
Endothelial dysfunction	Left ventricular hypertrophy
*Metabolic syndrome	Ischaemic heart disease
	Cardiac dysrhythmias
	Congestive heart failure

OSA: obstructive sleep apnoea

\* Not well documented in children or data showing conflicting results

mediated through metabolic abnormalities associated with insulin resistance. Some cardiovascular complications may be initiated or potentiated by OSA, which is often associated with obesity. The long-term health issues are serious and carry a heavy burden both clinically and financially. This then underscores the importance of prevention of obesity in children and adolescents. Prevention of obesity or early management of obesity can abate or reverse almost all of the cardiovascular consequences of obesity. One important issue is to convince parents and the general public to recognise the health consequences of obesity in young children and adolescents, develop greater awareness for this condition and be proactive in the prevention and early management of obesity in the young. This is an objective that requires collective effort between the medical profession, government and the public.

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