CHAPTER II

LITERATURE REVIEW

Adolescent idiopathic scoliosis

Scoliosis is an orthopedic condition effecting spinal alignment, growth, and function. The most common scoliosis is idiopathic scoliosis which has an unknown etiology (4). It commonly occurs in adolescence so called adolescent idiopathic scoliosis (AIS). The female to male ratio is not different for the small curve, but this ratio is increased (8 - 10 girls : 1 boy) when the curvature is greater than 30° (7, 13). The rate of bone growth in female puberty is more rapidly than those in male (7). This causes the dominant curve in girls to be more progressive than in boys.

The prevalence of AIS approximately develops two to four percent in children aged 10 to 16 year in North American (14, 15). The AIS prevalence in Singapore was 0.93 percent (16). Unfortunately, the epidemiology of AIS in Thailand has not been existed. Even thought there is no specific number of Thai female AIS, a few patients with AIS are consulted the physical therapist at Maharaj Nakron Chiang Mai hospital, Chiang Mai, Thailand, every week.

According to the onset of scoliosis, idiopathic scoliosis is classified into three sub-groups (3, 5, 19). Infantile scoliosis has onset before three years old and juvenile scoliosis is first diagnosed between four to 10 years old. Lastly, AIS is found from age of 11 to 18 year (17).

The other classification is based on the spinal deformity. The Scoliosis Research Society (SRS) has defined scoliosis by using the Cobb method (13) measuring the lateral deviation as shown in anterioposterior X-ray film (18). This method is widely used in clinics. The Cobb method provides the Cobb angle measured by measuring angle where the perpendicular line of the upper margin of the highest vertebra of curvature and the perpendicular line of the lower margin of the bottom vertebra of curvature is intersected (Figure 1). This angle is measured in one plane only whereas the deformity is occurred in three dimensions. The error was found between three to five degrees within the same observer (19).

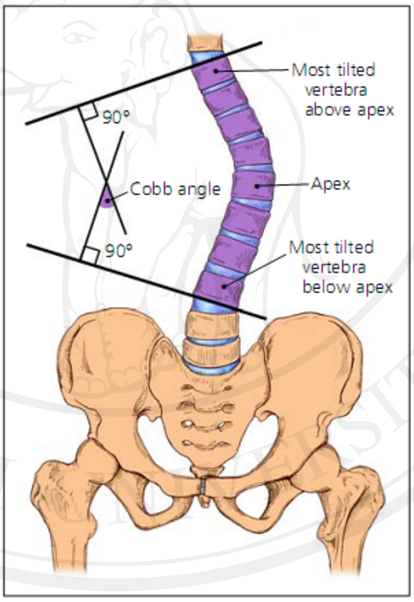

Figure 1. The Cobb method of measuring curvature (Greiner (19))

In this review, the classification of the AIS severity is determined by using the Cobb angle, according to SRS (12, 17, 20). When the Cobb angle is less than 10°, it is considered as normal. For the mild scoliosis, the Cobb angle is between 10° to 30°.

For the moderate scoliosis, the Cobb angle is from 30° to 45°. For the severe scoliosis, the Cobb angle is greater than 45°.

Also, scoliosis can be classified based on the spinal level involved (1). It can be classified into four types of scoliosis: 1) thoracic scoliosis, 2) thoracolumbar scoliosis, 3) lumbar scoliosis (C-curve), and 4) double major scoliosis (S-curve).

Structural deformity and mechanical change

The scoliosis is described by transformation in three-dimensional planes (5, 6, 13, 20, 22). The lateral deviation in the frontal plane combines with the rotation of the vertebral in the horizontal plane body resulting in the change of rib cage shape, concave and convex curvatures. If thoracic vertebrae are involved, the ribs are posteriorly displaced on convex side causing widening on the rib space. The others are anteriorly moved on the concave side causing narrowing on the ribs space. In some cases, the scoliosis may be combined with hypokyphosis (20). The apparently kyphosis called "rib hump" arises as the result from rib prominence in the convex-side. The thoracic cavity and length of respiratory muscle are involved. Tension generated by the respiratory muscles may reduce. Consequently, the ventilatory pump may be impaired.

Diaphragm plays an important role during inspiration which is an active process (21, 22). Their origin is from the lower ribs and inserts into the central tendon of each side of the thoracic cavity. When the diaphragm is contracting, the abdominal contents are pushed downward and forward. The lower ribs are moved forward and upward to increase thoracic volume. In addition, expiration is the passive process because of the property of elastic tissues of chest wall except during heavy exercise.

Pulmonary measurements

The pulmonary measurements in this review are composed of the flow-volume loop, maximum voluntary ventilation (MVV), maximal inspiratory, and expiratory pressure (MIP and MEP).

The flow-volume loop is used to measure both lung capacity and volume by using spirometer (23, 24). The purposes of the test are for screening, diagnosing, and following-up the ventilatory pump. The subject cooperation during the tests is required because the tests are effort dependence (23). Age, gender, weight, height, and ethnicity can contribute to the results. The test maneuver requires at least three trials, but not more than eight trails. The major measurement outcomes are forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), percent predicted forced vital capacity (pred FVC), percent predicted forced expiratory volume in one second (pred FEV_1), and the FEV_1/FVC ratio. These variables can be used to identify ventilatory pump problems whether it is the restrictive or the obstructive type. The best value on each variable is used. The standard measurement and the quality assurance for the flow-volume loop are already existed (23).

The criteria for restrictive pulmonary is indicated by pred FVC according to the American Thoracic Society (ATS). The restrictive severity can be divided into three groups: 1) mild restriction (FVC < 80 % predicted, $FEV_1/FVC > 0.8$), 2) moderate restriction (FVC < 65 % predicted, $FEV_1/FVC > 0.8$), and 3) severe restriction (FVC

< 50 % predicted, $FEV_1/FVC > 0.8$) (25). According to The Global Initiative for Chronic Obstructive Lung Disease (GOLD), obstructive pulmonary disease can be classified into four levels: 1) mild obstruction ($FEV_1 \geq 80$ % predicted, $FEV_1/FVC < 0.7$), 2) moderate obstruction (50 % $\leq FEV_1 <$ 80 % predicted, $FEV_1/FVC < 0.7$), 3) severe obstruction (30 % $\leq FEV_1 <$ 50 % predicted, $FEV_1/FVC < 0.7$), and 4) very severe obstruction ($FEV_1 <$ 30% predicted, or $FEV_1 <$ 50 % predicted plus chronic respiratory failure, $FEV_1/FVC < 0.7$).

Additional variables, which can imply the ability of the ventilatory pump is MVV. The MVV is indicated the breathing capacity at rest. It is normally performed for 6 second, 12 second, or more (26). Then, it will be extrapolated for 1 minute. During the test, the structures related to ventilatory pump such as chest wall, lung, respiratory muscles, and etc. have to work in concert. In normal subjects, MVV is greater than maximal minute ventilation (VE_{max}) for 30 to 40 percent (26). It implies that the respiratory system has a reserved capacity for about 30 to 40 percent. The MVV maneuver requires at least two acceptable maneuvers and the best value will be used. The standard procedure for MVV is already available (23). There are no reference equations for Thai population.

The MIP and MEP are the maximal pressure generated at the mouth during the inspiration and the expiration. They are used to determine the respiratory muscle strength. According to length-tension relationship, respiratory muscle strength is depended on the lung volume. The MIP and the MEP are measured at the residual volume (RV) and total lung capacity (TLC), respectively. The standard measurement and quality assurance for MIP and MEP are already existed (27). The MIP and the

MEP maneuvers are simple to use in all children, adolescents, adults, and elders. Gender, age, smoking habit, and activity level can make a variation on the respiratory muscle strength (28). The test maneuvers have to be at least five trials for both MIP and MEP and at least one minute rest in between is required. The learning effect is up to the fifth to ninth trials (29). The maximum value of three maneuvers with less variation than 20 percent is recorded.

Functional capacity and the six-minute walk test

The functional capacity refers to the ability of a person to perform aerobic work (30) resulted form the integrated work of the musculoskeletal, the cardiovascular, and the pulmonary system (31, 32). The functional capacity, exercise capacity, and exercise tolerance are considered synonym which implies the individual maximal effort during the given maximal exercise test. They are also used to express an individual's capacity to perform sub-maximal activity test (30).

The maximal oxygen uptake (VO_{2max}) is used to indicate the exercise capacity and the peak point of an individual's physiological limitation. VO_{2max} is defined as a plateau in oxygen uptake (VO_2) while the exercise intensity is increased. In cardiovascular and pulmonary diseases, the term peak oxygen uptake (peak $VO_{2)}$ is commonly used in clinical settings to express exercise capacity.

The VO_{2max} is affected by age, gender, conditioning status, presented individual disease, or medications (30, 33). The aerobic capacity decreases on average three to six percent per decade in young individuals (aged 20-39 year), and more than 20 percent per decade in the elderly (aged 70 years and older). Males show 10 to 20 percent greater exercise capacity than females at any age. The non-athletes have a declining average rate of exercise capacity 10 percent per 10 years (30).

The six-minute walk test (6 MWT) is modified from the 12-minutes walk test which is assigned for evaluate physical fitness of healthy individuals (34). This is due to the high intensity level of the 12-minute walk test which is difficult for patient with low exercise capacity and patients with cardiorespiratory diseases (35). The 6 MWT is developed to evaluate the functional capacity by measuring six-minute walk distance (6 MWD) (31, 36-38). The physiological variables such as heart rate (HR), blood pressure (BP), oxygen saturation ($SatO_2$), and level of fatigue and dyspnea before and after the test are measured. They can be used as the secondary outcomes (31, 39). The walking distance can be reported as raw score, change of raw score, or change of percent predicted value. The 6 MWT is commonly used in clinical setting because it is simple, inexpensive, and time-cost effective (31, 36, 40). The limitation of 6 MWT does appear in identifying the influenced body system or body organ on the functional limitation (31).

The 6 MWT standard protocol was published by the American Thoracic Society (ATS) (31). The standardized protocol recommends that 6 MWT should be performed indoors on a hard flat at least 30 meters straight hallway. However, the guideline for the 6 MWT states that the courses length 15 to 50 meters (50 to 164 ft.) did not show any significant effect on the result. Testing on a treadmill is not recommended even though it would save space and allow the constant variable monitoring. To perform the test, subjects will be asked to walk for six minutes and try to cover the distance as much as they can. At least two trials of the test are recommended and the farthest 6 MWD is recorded.

The reliability of the 6 MWT has been proven in several populations (41-44). The test-retest reliability in patients with heart failure at the baseline, 18 weeks, and 43 weeks were very good (intraclass correlation coefficient [ICC] = 0.90, 0.88 and 0.91, respectively) (41) as well as in the advanced heart failure populations (ICC = 0.96, $p < 0.05$) (45). The reliability was also found in the healthy elderly group (44). In healthy children aged 12 to 16 years, the test-retest reliability showed that ICC was excellent over separated 18 days (ICC = 0.94, range 0.89 to 0.96, $p < 0.05$) (42). The 6 MWT was also reported to be reliable and valid in both healthy children (42, 46, 47) and ill children (12, 48-50). At this present, there is no study of the 6 MWT reliability in the AIS but the 6 MWT was recently used to evaluate changes of functional capacity after the aerobic exercise rehabilitation in individuals with AIS (12).

The 6 MWD confounding factors are age, sex, height, body weight, motivation, medication taken, oxygen supplementation, course layout, and learning effect (31, 44, 46, 48, 51, 52). Elderly, overweight, female gender, impaired cognitive function, short leg length, cardiopulmonary disease, and short walking path can reduce the 6 MWD. In contrast, the 6 MWD tends to increase with increased height as well as in male gender. Moreover, taking medication, oxygen supplement, and test experiences may induce the greater distance from the test.

Recent studies found that the 6 MWD showed positive correlation with age in children ($r = 0.105$, $p < 0.01$) whereas there was negative correlation with age in adults ($r = -0.51$, $p < 0.05$) (46, 48, 51). Li et al (46) reported that taller adults have a larger stride length producing the greater distances. The author also stated that the body mass index (BMI) showed significant reduction of 6 MWD (46) in both males and females ($r = -0.797$ to -0.806, $p < 0.01$).

Additionally, the learning effect plays an important role in increasing the 6 MWD. The greater distance from learning effect may be observed at the second trial (43). The 6 MWD was statistically significant positive correlation between first to third trails within the same day ($r = 0.90 - 0.98$, $p < 0.001$) (52). Furthermore, there was also the positive correlation within-subject reproducibility for 6 MWD in the first and the second trial ($r = 0.98$, SD/mean 4.2 %) (53). In order to limit the learning effect, Karvio et al (54) suggested that two trials were accepted for 6 MWT. Thus, the practice should be made to reduce learning effect.

Since the physiological variables are interested in 6 MWT, the effect of the environment should be considered (44, 54, 55). The 6 MWT was performed indoor and outdoor where temperatures were 21° ± 3° Celsius. The results showed that there were no statistically significant difference in HR, the $SatO_2$, dyspnea, and the distances (55); however, the author suggested that more diverse temperature should be investigated. Additionally, 6 MWT should be performed at the same time of the day because of diurnal change (44, 54). The HR was significantly higher in the afternoon than in the morning (128.2 ± 4.1 vs. 121.8 ± 4.1, $p < 0.001$, respectively) in healthy elderly and chronic heart failure patients.

The 6 MWT can be applied to test functional capacity (single measurement) or changes in functional capacity due to an intervention (pre- and post-treatment comparisons) in patients with chronic obstructive pulmonary disease (COPD) (37, 39), heart failure (45, 56), fibrotic interstitial pneumonia (53), cystic fibrosis, peripheral vascular disease, and elderly patients (31, 34, 42).

Individuals with low exercise capacity respond to 6 MWT as the high-intensity exercise (33, 39, 42). In healthy elderly subjects, the intensity of 6 MWT was 79.6 ± 4.5 percent of the VO_{2max}, 85.8 ± 2.5 percent of the maximal heart rate (HR_{max}), and 78.0 ± 6.3 percent of reservation heart rate ($HR_{reserve}$) (54). In patients with moderate to severe COPD, the maximal sustainable walking speed and the peak VO_2 increased to the plateau in the last three minute of the test. If the 95 percent to 105 percent of peak walking speed were performed, 6 MWT could produce the peak VO_2 comparable to maximal stress test. The peak VO_2 during 6 MWD was not different from the peak VO_2 during incremental cycle ergometry in stable COPD (37).

The positive correlation between the 6 MWD and the oxygen consumption was found ($r = 0.93$, $p < 0.001$) (39). The significant correlation between 6 MWD and VO_2 ($r = 0.64 – 0.78$, $p < 0.0001$) were reported in patients with heart failure (45, 56), fibrotic interstitial pneumonia (53), cystic fibrosis, peripheral vascular disease, and elderly (31, 34, 42, 45, 53).

The reference equations of 6 MWD in Caucasian female adolescent are: 1) 661.9 ± 56.7 m. for aged nine to11 year, 2) 663 ± 50.8 m. for aged 12 to 15 year, and 3) 664.3 ± 49.5 m. for aged 16 or older (48). However, Lammer et al (47) stated that the 6 MWD was not significantly different among Caucasian children, Asian/Asian-Caucasian, and Afro-Caribbean/Afro-Caribbean-Caucasian aged four to 11 year. In addition, the standard reference distance for 6 MWT in Chinese female aged seven to 16 years is 642.7 ± 58.9 m. (46). At this point, there is no Thai adolescent reference equation. Previous study also showed that there was no difference in distance between boys and girls aged four to 11 year (47). These may be because the rate of growth in children in these ages may be related to an increase in height. Girls tend to grow in height between the ages of 10 to 15 while boys show the first physical changes in height between the ages of 10 to 16 (57).

Adolescent idiopathic scoliosis and ventilatory pump impairment

In AIS individuals with thoracic vertebrae involved, the origins and insertions of diaphragm and all accessory muscles (i.e. external intercostals muscle, pectoralis minor, the scalene and the sternocleidomastoids) are changed. This results in the mechanical disadvantage of the respiratory muscles to generate the tension, and eventually, the ability to ventilate is impaired (24).

The individuals with AIS are known for having the restrictive lung disease. Significant reduction of FVC was found across the AIS severity, thus restrictive lung in this AIS population is existed. However, it is not the case when the correlation between the Cobb angle and the FVC was evaluated. In any degrees of Cobb angle, the FVC in some patients were still normal but some were abnormal (6, 8, 58). The significant correlation was found in moderate to severe AIS ($r = -0.36$ to -0.30, $p < 0.05$), whereas it was not in the mild AIS (59). The pulmonary function tests may not be sensitive to determine this correlation. This may be because the Cobb angle is measured only one plane, whereas the deformity of AIS simultaneously occurs in three planes. Recently, using computed tomography (CT) scan, the significant correlation between the lung volume and the spinal curvature in a wide range of scoliosis was found (20). However, the CT scan is not commonly used in clinical setting because it is expensive.

Several studies showed that pred FEV_1 in the AIS was significantly reduced, but FEV_1/FVC was not lower than 70 percent (8, 10). According to GOLD guidelines, it is not represented obstructive lung diseases across the severity groups. However, the study reported that reduction of air taping and airway resistance post bronchodilator was found in moderate to severe AIS (10). Some degrees of airway obstruction may impair the ventilatory pump in these AIS.

The MVV is used to indicate breathing capacity at rest. Some individuals with mild AIS showed MVV reduction. During exercise, the VE_{max} in mild to moderate AIS was significantly lower than the healthy individuals (66.7 ± 12.3 vs. 82.3 ± 10.7 L/min, $p < 0.05$) (9). Also, the greater respiratory rate was found in this group (54 ± 8 vs. 47 ± 8 bpm, $p < 0.05$). This revealed that ventilatory pump is not efficient in the pathologic group. Thus, dypnea may occur at high exercise intensity, but not during low exercise intensity like performing daily activities. However, the significant correlation between Cobb angle and MVV was not found across the severity (58, 59).

Comparing to normal individuals, the MIP and MEP were significantly reduced in moderate and severe AIS, but it was not in the mild group (11, 60). This may be because in mild degree of the AIS, the mechanical disadvantage of respiratory muscles may not significantly compromise the force production. Additionally, Cobb angle was neither associated with MIP, nor with MEP in mild AIS. Correlation between Cobb angle and respiratory muscle strength (MIP and MEP) in moderate and severe AIS has not been reported.

In conclusion, the individuals with AIS may have mixed ventilatory pump impairment: restrictive and obstructive type. The ventilatory pump impairment seems to be associated with the AIS severity.

Adolescent idiopathic scoliosis and cardiovascular impairment

Deconditioning in AIS is defied as "…less active and participate less in sports and exercise than their age and sex-match peer…". (8). It can possibly be a cause of cardiopulmonary impairment in severe AIS. To compare with normal subjects, mild to moderate AIS showed statistically significant lower HR at anaerobic threshold (167 ± 16 vs. 180 ± 5 bpm, $p < 0.05$) (12). This suggested that the individuals with mild to moderate AIS were less fit than the normal subjects. The untrained individuals with severe AIS also showed that HR was statistically significant decreased after aerobic training (108 ± 12.31 vs. 96 ± 8.67 bpm, $p < 0.0001$). This implies that the severe AIS group is in decondition and aerobic exercise training can regain their fitness level. Systolic and diastolic blood pressure at maximal exercise in AIS subjects were not difference from the healthy group. Up to date, the data on cardiovascular impairment in AIS are limited. It is not known whether the AIS severity is associated with the cardiopulmonary impairment. However, cardiovascular impairment seems to be presented in individuals with AIS.

Adolescent idiopathic scoliosis and functional limitation

Functional capacity means the ability to perform the necessary tasks or ability to achieve activities in daily life. Functional limitation may be the results of the musculoskeletal, the pulmonary, and the cardiovascular impairment in AIS. The 30-year follow-up in untreated patients with scoliosis showed that 29 percent of 219 scoliosis had shortness of breath on a daily basis (61).

During maximal exercise stress test, the individuals with mild to moderate AIS had lower VO_{2max} than healthy subjects (38.6 ± 6.2 vs. 49.9 ± 7.5 ml/kg/min; $p < 0.001$) (9). In severe AIS, the 6 MWD was statistically improved for approximately 129 m. after 4-month aerobic exercise training (400.71 ± 49 vs. 529 ± 65.19 m., $p < 0.0001$) (12). The deconditioning may partially reduce their functional capacity. Fortunately, their functional capacity can be regained by physical training.

The spinal deformity is progressed as aging. The AIS life expectancy is reported about 65 years old (62). This means that the huge impact of deconditioning can occur as the deformity progressed throughout the AIS life. Also, chronic back pain, poor self-image, and deteriorated mental status in AIS are reported. These may aggravate their deconditioning and consequently functional limitation. Although the AIS patients in Thailand may not be a large population, the best clinical practices based on scientific evidences should be provided. However, the evidences related to cardiopulmonary impairment and functional limitation are limited. More research needs to be done. Up to date, the effects of scoliosis severity on the cardiopulmonary impairment and functional capacity have not been made. Furthermore, the relationship among the musculoskeletal, the cardiovascular, the pulmonary impairment, and the functional limitation has not been established.