Challenges and Long-Term Management of Patients with Craniofacial Clefts in Thailand

Bowonrnsilp Chowchuen MD, MBA*, Palakorn Surakunprapha MD*, Prathana Chowchuen MD**, Keith Godfrey MDS, Dr.Dent***

* Division of Plastic Surgery, Department of Surgery, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand
** Department of Radiology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand
*** Department of Orthodontics, Faculty of Dentistry Khon Kaen University, Khon Kaen, Thailand

Objective: To report challenges and long-term management of patients with craniofacial clefts, treated at Srinagarind Hospital, Khon Kaen, Thailand.

Material and Method: Patients who were treated at Srinagarind Hospital, between 1993 and 2001. A review of data was performed including general information, classifications, photographs, radiographic findings, dental records, reconstructive surgeries, and long-term management.

Results: A total of 20 patients were recruited; six males and 14 females, grouped into six median, two paramedian and 12 oblique clefts. Age of the first treatment ranged from one to 39 years, age of the last follow-up ranged from 11 to 48 years and the range of follow-ups was 11 to 24 years. The reconstructive procedures included a variety of techniques of plastic surgery for soft tissue repairs and bone grafting for facial reconstructions. Four patients with median clefts and paramedian clefts died. One patient lost to follow-up. Fifteen patients were followed-up and the results were satisfying.

Conclusion: Diagnosis, evaluation, and treatment of clefts and craniofacial deformities are complex. The proper management is challenging because of socioeconomic, cause difficulties in follow-ups according to the planned protocol. Other associated anomalies are important. Protocols with well-co-ordination of an interdisciplinary team in Craniofacial Center and continuing evaluation at appropriate schedule and age group until completion of facial growth are critical factors. Establishment of a foundation and comprehensive care model with families, local health professionals and school will benefit the most to this group of patients.

Keywords: Craniofacial clefts, Challenges, Long-term management, Thailand

J Med Assoc Thai 2015; 98 (Suppl. 7): S38-S46
Full text. e-Journal: http://www.jmatonline.com

Craniofacial clefts are abnormal disfigurements of cranium and face with deficiencies, excesses, or normal amount of tissue occurring along a linear region\(^1\). The incidence is rare, estimated widely from 0.75 to 5.4\(^2\) and mostly in developing countries. There are challenges for classification, evaluation, multidisciplinary management, surgical reconstruction, long-term management and measuring the outcomes of these birth defects. The reconstructive procedures of craniofacial clefts are extremely difficult in terms of achieving long-term goals in completion of rehabilitation, in dimension of esthetics, functional, spiritual and developmental aspects. The results have to be evaluated at the time of complete facial growth in adolescent age or when satisfied by patients and their family. Many of the literatures reported the results of solitary cases\(^3-5\), however, there is little information of the report for clinical series and long-term management of patients.

The purpose of this study was to report the challenges and long-term management of patients with craniofacial clefts treated at Srinagarind Hospital, Khon Kaen University, Thailand. The results from this study would be useful for future management of these patients.

Material and Method
The study included all patients with craniofacial clefts who were initially treated at Srinagarind Hospital between 1993 and 2001 based on clinical presentation and radiological reports. They were...
classified according to the Tessier’s classification\(^a\) as median clefts (cleft No. 0/14), paramedian clefts (cleft No. 1/13 and 2/12) and oblique clefts (cleft No. 3/11, 4/10 and 5/9). The cleft No. 0/14 were divided into a tissue deficiency type or holoprosencephaly and a tissue excess type or frontonasal dysplasia\(^b,c\). The following information was reviewed including general information, cleft classification, photographs, radiographic findings, dental records, reconstructive surgeries, and long-term management.

The study protocol was approved by the Ethics Committee of Khon Kaen University, according to the Helsinki Declaration. Written informed consent was obtained from each patient.

**Protocol for treatment**

Photographs, dental records and, if possible, a 3D Computer Tomography (CT) scan and Magnetic Resonance Imaging (MRI) were used to classify deformities, and evaluate the soft tissue and bony deformities, as well as other associated anomalies. The primary or secondary reconstructions were performed according to urgency of the deformities and appropriate age of the patients. The interdisciplinary team, including plastic surgeons, neurosurgeons, orthodontists, speech pathologists, radiologists, socials workers, psychiatrists and nurse co-ordinators provided their opinions on treatment plans. The needs and expectations of patients and their family were used for decision making on treatment.

**Results**

Twenty patients were recruited: six males and 14 females. Age ranged from one to 39 years. They were grouped into six median, two paramedian and 12 oblique clefts. Table 1 shows the details of these patients.

Eighteen patients received soft tissue repairs, including a variety of plastic surgical techniques and one tissue expansion. Five patients received bone grafting for facial and orbit reconstruction. Four patients died, including two patients of median cleft with holoprosencephaly and severe associated anomalies, one patient with median cleft with frontonasal dysplasia, and one patient with paramedian cleft, because of associated intracranial anomalies and sepsis. A cause of death in one patient was not identified. One patient lost to follow-up. Even though additional surgeries were recommended in some patients, satisfactory results were achieved in all of 15 patients who were followed-up.

**Patient report**

**Patient No. 2**

A female neonate presented with cleft No. 0/14 with holoprosencephaly, a single nostril, and associated cardiac malformation (Fig. 1). She developed birth asphyxia, jaundice and died from sepsis on the 27th day after birth.

**Patient No. 3**

A baby boy presented with cleft No. 0/14 median facial cleft with bifid nose, duplicated columella, significant of notching of the vermillion border, microphthalmia and microcephalus. CT scan revealed bony defects at midface and orbital hypertelorism. MRI revealed microphthalmia of right eye with associated agenesis of corpus callosum of the brain (Fig. 2).

**Patient No. 6**

A girl presented with a median cleft, bifid nose, widening of columella, and notching of the vermillion border. The nasal and lip correction was performed with satisfactory results at the age of 18 years (Fig. 3).

**Patient No. 7**

One of male twins presented with cleft No. 1/13, microphthalmus and microcephalus. CT scan revealed hypoplasia of maxillary antrum, hypertelorism and low lying of frontal lobe of the brain. Lip and soft tissue reconstruction with median canthopexy and palatoplasty was performed at the age of one year (Fig. 4). His cause of death was not identified.

**Patient No. 8**

A patient presented with left cleft No. 3, and right cleft No. 6 with left microphthalmos. Soft tissue reconstruction with tissue expander was performed at 1 year. He was lost to follow-up and at age 17 years, he still had some deformities but was satisfied with the treatment (Fig. 5).

**Patient No. 14**

A baby girl presented with coloboma of upper eyelids. Eyelid reconstruction was performed with subsequent revision at the age of ten years (Fig. 6).

**Patient No. 20**

A boy presented at the age of seven years with paramedian nasal cleft No. 2. Nasal reconstruction was performed. He was lost to follow-up; however, satisfactory results were achieved at the age of 22 (Fig. 7).
<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Name</th>
<th>Gender</th>
<th>Age of presentation</th>
<th>Province</th>
<th>Diagnosis</th>
<th>Surgical treatment</th>
<th>Age of the last follow-up (years)</th>
<th>Outcomes of the last follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NP</td>
<td>M</td>
<td>1993</td>
<td>Khon Kaen</td>
<td>No. 0/14, median cleft with holoprosencephaly</td>
<td>None</td>
<td>-</td>
<td>Dead</td>
</tr>
<tr>
<td>2</td>
<td>A</td>
<td>F</td>
<td>1997</td>
<td>Khon Kaen</td>
<td>No. 0/14, median cleft with single nostril</td>
<td>None</td>
<td>-</td>
<td>Dead</td>
</tr>
<tr>
<td>3</td>
<td>TI</td>
<td>M</td>
<td>1999</td>
<td>Chaiyaphum</td>
<td>No. 0/14, median cleft</td>
<td>Nasal and lip reconstruction</td>
<td>-</td>
<td>Dead</td>
</tr>
<tr>
<td>4</td>
<td>KW</td>
<td>M</td>
<td>1961</td>
<td>Nakhon Phanom</td>
<td>No. 0/14, median cleft</td>
<td>Nasal reconstruction</td>
<td>48</td>
<td>Satisfied</td>
</tr>
<tr>
<td>5</td>
<td>MM</td>
<td>F</td>
<td>1993</td>
<td>Khon Kaen</td>
<td>No. 1/13, Rt. paramedian cleft</td>
<td>Nasal reconstruction</td>
<td>20</td>
<td>Satisfied</td>
</tr>
<tr>
<td>6</td>
<td>PC</td>
<td>F</td>
<td>1992</td>
<td>Maha Sarakham</td>
<td>No. 0/14, tissue excess median cleft</td>
<td>Nasal reconstruction</td>
<td>18</td>
<td>Satisfied</td>
</tr>
<tr>
<td>7</td>
<td>WS</td>
<td>M</td>
<td>1998</td>
<td>Nong Bua Lam Phu</td>
<td>No. 2/12, Lt. paramedian cleft</td>
<td>Soft tissue and palatal reconstruction</td>
<td>-</td>
<td>Dead</td>
</tr>
<tr>
<td>8</td>
<td>AN</td>
<td>M</td>
<td>1993</td>
<td>Chaiyaphum</td>
<td>No. 5/9, rt. and No. 3/11, Lt. oblique cleft with Lt. anophthalmus</td>
<td>Soft tissue reconstruction with tissue expansion</td>
<td>20</td>
<td>Satisfied</td>
</tr>
<tr>
<td>9</td>
<td>CS</td>
<td>F</td>
<td>1991</td>
<td>Chaiyaphum</td>
<td>No. 3/11, Rt. oblique cleft</td>
<td>Soft tissue and bony reconstruction</td>
<td>21</td>
<td>Satisfied</td>
</tr>
<tr>
<td>10</td>
<td>SP</td>
<td>F</td>
<td>1977</td>
<td>Khon Kaen</td>
<td>No. 3/11, Rt. oblique cleft</td>
<td>Soft tissue and bony reconstruction</td>
<td>22</td>
<td>Satisfied</td>
</tr>
<tr>
<td>11</td>
<td>DP</td>
<td>F</td>
<td>1998</td>
<td>Roi Et</td>
<td>No. 3/11 Rt. and No. 5/9 Lt. oblique cleft</td>
<td>Soft tissue and bony reconstruction</td>
<td>16</td>
<td>Satisfied</td>
</tr>
<tr>
<td>12</td>
<td>YK</td>
<td>F</td>
<td>1994</td>
<td>Khon Kaen</td>
<td>No. 3 Rt. oblique cleft</td>
<td>Soft tissue and bony reconstruction</td>
<td>19</td>
<td>Satisfied</td>
</tr>
<tr>
<td>13</td>
<td>RC</td>
<td>F</td>
<td>1981</td>
<td>Sakon Nakhon</td>
<td>No. 3/11 Lt. oblique cleft</td>
<td>Soft tissue and bony reconstruction</td>
<td>29</td>
<td>Satisfied</td>
</tr>
<tr>
<td>14</td>
<td>LW</td>
<td>F</td>
<td>1999</td>
<td>Nong Bua Lam Phu</td>
<td>No. 3/11 bilateral oblique cleft, coloboma of both eyelids</td>
<td>Eyelid reconstruction</td>
<td>11</td>
<td>Satisfied</td>
</tr>
<tr>
<td>15</td>
<td>DC</td>
<td>F</td>
<td>1995</td>
<td>Chaiyaphum</td>
<td>No. 3/11 Rt. oblique cleft, Rt. eyelid coloboma</td>
<td>Eyelid reconstruction</td>
<td>15</td>
<td>Satisfied</td>
</tr>
<tr>
<td>16</td>
<td>WI</td>
<td>F</td>
<td>1990</td>
<td>Nakhon Phanom</td>
<td>No. 3/11 Rt. and No. 5/9 Lt. oblique cleft</td>
<td>Soft tissue and bony reconstruction</td>
<td>22</td>
<td>Satisfied</td>
</tr>
<tr>
<td>17</td>
<td>PS</td>
<td>F</td>
<td>1996</td>
<td>Khon Kaen</td>
<td>No. 3/11, bilateral oblique cleft, bilateral eyelid coloboma</td>
<td>Eyelid reconstruction</td>
<td>15</td>
<td>Satisfied</td>
</tr>
<tr>
<td>18</td>
<td>JR</td>
<td>F</td>
<td>1994</td>
<td>Maha Sarakham</td>
<td>No. 3/11, bilateral oblique cleft</td>
<td>Soft tissue reconstruction</td>
<td>-</td>
<td>Lost to follow-up</td>
</tr>
<tr>
<td>19</td>
<td>CP</td>
<td>F</td>
<td>1995</td>
<td>Kalasin</td>
<td>No. 3/11, bilateral, oblique cleft, Rt. upper and lower eyelid coloboma</td>
<td>Eyelid closure, Soft tissue reconstruction</td>
<td>15</td>
<td>Satisfied</td>
</tr>
<tr>
<td>20</td>
<td>NK</td>
<td>M</td>
<td>1992</td>
<td>Chaiyaphum</td>
<td>No. 2 Lt. paramedian cleft, nasal cleft</td>
<td>Nasal reconstruction</td>
<td>22</td>
<td>Satisfied</td>
</tr>
</tbody>
</table>

Rt. = right; Lt. = left
Frontal, intraoral views and dental model of patient No. 2, the female neonate presented with cleft No. 0/14 with holoprosencephaly and a single nostril.

Photos, dental model CT scan and MRI of the baby boy presented with cleft No. 0/14 median facial cleft with bifid nose, duplicated columella, significant of notching of the vermillion border, microphthalmia and microcephalus.

Photos, dental model and CT scan of a girl presented with a median cleft.

Photos of the one of male twins presented with cleft No. 1/13, microphthalmus and microcephalus.

Discussion

The classifications of craniofacial clefts are based on anatomic findings by Tessier (8), embryonic basis by Van der Meulen (9) and by dividing the clefts into four categories: the oro-nasal cleft, the oral ocular clefts, the lateral facial clefts, and the orbital cranial clefts (10). However, the Tessier’s classification is currently accepted as the standard classification. The etiology has been focused on the nutrition problems and genetic factors (10).

Interdisciplinary team set up in Khon Kaen University since 1999 to provide comprehensive patient care with centralization and long-term treatment plan (11). A protocol was adapted according to cleft deformities, age group, team consultation, holistic outcomes, and the consideration of growth and long-term effects. Plain film, CT scan and MRI are important tools for evaluation of the deformities associated anomalies, planning of the surgical reconstruction and assessment of outcomes (4, 12-14). CT scans are used to evaluate soft tissue and bony structures during primary and secondary reconstruction, details of anomalies of the midface and in patient with frontonasal dysplasia (15). MRI scans are used to evaluate associated intracranial anomalies in median and paramedian clefts. For patient No. 3, CT scan revealed bony defects involving frontal, nasal and maxilla with fronto-ethmoidal defect and orbital hypertelorism and MRI revealed congenital...
Fig. 5 Pre- and post-operative photos of a patient presented with left cleft No. 3, and right cleft No. 6 with left microphthalmos, treated with soft tissue reconstruction with tissue expander.

Fig. 6 A girl patient presented with coloboma of upper eyelids. Eyelid reconstruction was performed with subsequent revision at the age of ten years.

Fig. 7 Pre- and post-operative photos of a boy presented with paramedian nasal cleft No. 2.

Microphthalmia of right eye with agenesis of corpus callosum. For patient No. 10, CT scan revealed bony defects of right orbit and maxilla. Patients with median cleft and holoprosencephaly may require detailed imaging of face and brain. A rapid prototyping technique may be used for pre-operative prefabricate templates of oblique clefts(10).

Early orthopedic treatment of oblique clefts has been reported(17) and provided assistance with oral feeding. Individual problems in the continuing dental and orthodontic management were addressed such as highly variable developing dental condition. Patients with more severe clefts may require different forms of prosthesis and oral implants(18).

Craniofacial clefts require corrections of both soft tissue and skeletal deformities. The urgency depends on the impact of functional and anatomical integrity such as maintaining the respiratory and correcting the exposure of eye globe(19). In our study, an early reconstruction of eyelids was performed in patient No. 15, 17 and 19. Integrated concepts should be used for primary reconstruction with considering all deformities related to craniofacial clefts and associated anomalies. The principles of soft tissue reconstruction depend on characteristics of cleft and reconstruction of all essential soft tissue in restoration of functions and anatomical landmarks. Tissue expansion may be used in severe cases to provide more tissue, allow tension-free reconstruction and improve esthetic results(20) which was used in patient No. 8.

Median clefts (cleft No. 0/14), involving the midline, were classified into tissue deficiency type or holoprosencephaly, tissue excess type or frontonasal hyperplasia, and the abnormal clefting with normal tissue volume (dysraphia)(21). These clefts are reconstructive challenges, requiring multiple operations throughout life and often have unpredictable growth(22). They may manifest as hypotelorism to more severe forms with absent nose, brain anomalies and mental retardation. Most of the patients die within the first three months and rarely live to the end of infancy.
period. It is recommended to wait until the patient is one or two years old before corrective surgical procedure is considered and/or performed\(^{23}\). They are also at high risk of developing hypopituitarism\(^{24}\). Cleft No. 0/14 was tissue excess type or frontonasal dysplasia, which may be presented with hypertelorism, bifid nose, and mental retardation\(^{25}\). In our study, the surgical correction of hypertelorism was performed in patient No. 3.

Cleft No. 1/13 and 2/14 were paramedian clefts. These anomalies are different and surgical procedures may include nasal reconstruction and the correction of orbital hypertelorism\(^{26,27}\).

Cleft No. 3/11, 4/10 and 5/0 were oblique clefts. Cleft No. 3/11 may be the most common type. The challenges are short nose, deficiency of soft tissue between the alar base and lower eyelid, disrupted lower canaliculus, coloboma of medial part of lower eyelid and microphthalmus. Cleft No. 4/10 was one of the rare clefts\(^{14}\). The challenges are cleft of the upper lip, lateral to the nasal ala, and extention into lower eyelid lateral to the inferior punctum. Anophthalmus may also be reported\(^{28}\).

A surgical correction for cleft No. 3/11 and No. 4/10 has been advised\(^{29-32}\), including the use of interdigitating skin flaps along the line of the facial cleft. Rotation advancement cheek flap may be used subsequently to improve esthetically favorable results\(^{33}\). Cleft No. 10 may be implicated by the presence of coloboma of the middle third of the upper eyelids and eyebrows\(^{34}\). In our study, coloboma reconstruction of bilateral cleft No. 10 was performed in patient No. 15, 17 and 19. Cleft No. 5/9 were the rarest clefts and their challenges are cleft just medial to the oral commissure and passes into the lateral half of lower eyelid\(^{35}\). The early repair with proper soft tissue and bony reconstruction is recommended\(^{36}\).

Combined clefts and associated anomalies are the groups with more challenges\(^{37,38}\). The secondary reconstruction and bony surgery depend on their severity. Many studies recommend bone grafting approximately at the age of five years\(^{31,39-42}\). Calvarial bone grafts are used to fill the cleft and alveolus and for onlay grafts to maxilla, orbital rim, orbital floor, and pyriform rim\(^{30,43}\). Early bone grafting may be performed on severe clefts\(^{14}\). Lacrimal drainage surgery is performed to correct the problems of epiphora. The long-term results are challenges to be evaluated. Early soft tissue corrections may be performed for the scars in facial units. Esthetic subunit reconstruction may be performed before school age and bone grafting during mixed dentition period\(^{44,45}\).

The proper management of these clefts is challenging because of socioeconomic problems. These problems cause difficulties in follow-ups according to the planned protocol. In addition to hospital-based management, the establishment of foundation and comprehensive care model with families, local health professionals and school, will benefit the most to this group of patients.

There is limited information in the literature about long-term outcomes and optimal results of craniofacial clefts. This study, however, shows strengths in reporting series of long-term management and outcomes. Some limitations in this study are due to unavailability of complete treatment data and follow-ups. The treatment of craniofacial clefts in developing countries is constrained because of economic and health care facilities factors to complete follow-ups and treatment at the optimal period of growth.

**Conclusion**

Diagnosis, management, and treatment of clefts and craniofacial deformities are complex and require coordinated care and comprehensive management. Holistic care, consideration of patient’s and family’s needs and expectations, and the collaboration with health policy and school are important. Well-coordinated protocols of an interdisciplinary team in Craniofacial Center and continuing evaluation with appropriate scheduling and age groups until commencement of speech and completion of facial growth are critical factors for successful treatment.

**What is already known on this topic?**

Craniofacial clefts are abnormal disfigurements of cranium and face with deficiencies, excesses, or normal amount of tissue occurring along linear region. The incidence is rare, and mostly in developing countries. The reconstructive procedures of these clefts are extremely difficult in terms of achieving long-term goals.

**What this study adds?**

This study presents long-term management and results of patients with craniofacial clefts Thailand. There is little information on the report for clinical series and long-term management of patients. The limitations of their management and the satisfactory results are demonstrated. The results from this study could be useful for future management of these patients.
Acknowledgement

The present study was supported by the Tawanchai Foundation for Cleft Lip-Palate and Craniofacial Deformities and the Center of Cleft Lip-Cleft palate and Craniofacial Deformities, Khon Kaen University, in Association with the Tawanchai Project. The authors wish to thank Dr. Radhakrishnan Muthukumar for his assistance with the English-language presentation of the manuscript.

Potential conflicts of interest

None.

References


32. Chen PK, Chang FC, Chan FC, Chen YR, Noordhoff MS. Repair of Tessier No. 3 and No. 4 craniofacial clefts with facial unit and muscle repositioning by midface rotation advancement without Z-plasties. Plast Reconstr Surg 2012; 129: 1337-44.


ความท้าทายและการคุณลักษณะในผู้ป่วยที่มีภาวะการดวงวายของศีรษะและใบหน้าในประเทศไทย

บาร์บารา เขอร์น์ ช์, พลตร. สุรศักดิ์ ประทาน, เขอร์น์ ช์, Keith Godfrey

วัตถุประสงค์: เพื่อรายงานความท้าทายและการคุณลักษณะในผู้ป่วยที่มีภาวะการดวงวายของศีรษะและใบหน้าที่ได้รับการรักษา ในโรงพยาบาลศิริราช คณะแพทยศาสตร์ มหาวิทยาลัยรามคำแหง ประเทศไทย

วัตถุประสงค์: ผู้วิจัยมีการรายงานความท้าทายและการคุณลักษณะในผู้ป่วยที่ได้รับการรักษาในโรงพยาบาลศิริราชระหว่างปี พ.ศ. 2536 โดยการทบทวนข้อมูลที่ไป

การจำแนกชนิด ภาคพื้น ภาคบริสุทธิ์ การบันทึกทางทันตกรรม ชนิดของการติดเชื้อสาร และการคุณลักษณะ

ผลการศึกษา: ผู้ป่วยทั้งหมด 20 ราย เป็นชาย 6 ราย หญิง 14 ราย แบ่งเป็น ภาวะการดวงวาย และภาวะการการเวียน

ภาวะเวียน 12 ราย ผายของการบริการเติมเต็มสุขภาพ 1-39 ปี ผายของการบริการเติมเต็มสุขภาพ 1-24 ปี ผายของการิตติการรักษา

กระรุกเป็นดี 11-24 ปี ผายการิตติการรักษาได้แก่ รักษาดังกล่าว ทางศูนย์พระมหากษัตริย์ในระดับทวีปและสัมภัย

เพื่อศึกษาสรุป拢มาผู้ป่วยที่มีภาวะการดวงวาย และภาวะการเวียน ركز 4 ราย เซียร์ร์ ผู้ป่วย 1 รายขาดการิตติการรักษา ผู้ป่วย 15

รายได้รับการิตติการรักษาและมีความพึงพอใจในผลการรักษา

สรุป: การวิจัย การประเมิน และการรักษาผู้ป่วยที่มีภาวะการดวงวายและใบหน้าเป็นสาเหตุของการเดิน การเดินที่มีการเปลี่ยนแปลงอย่างมาก ผ่านการ

การตรวจร่างกาย ทำให้การรักษาการมีการเปลี่ยนแปลงทางการรักษาให้เหมาะสม ภาวะการเวียนไม่สามารถแก้ไข

การรักษา รวมถึงการป้องกันและประเมินผู้ป่วยตามชายแดน

ที่เหมาะสม แจ้งผู้ป่วยได้เป็นผู้ที่มีสิทธิ์ได้รับการรักษาทางการรักษาเป็นผู้ป่วยที่มีความสุขบุญคุณ การจัดคู่มือการรักษา

การสร้างการมีการดูแลสุขภาพแบบร่วมกับครอบครัวผู้ป่วย

ที่มีสุขภาพดีขึ้นและผู้ป่วยจะเป็นประโยชน์มากในการผู้ป่วยกลุ่มนี้