SURGICAL MANAGEMENT OF STERNAL TUMORS IN NATIONAL CANCER INSTITUTE
(clinicopathological study of sternal tumors)

Thesis

Submitted for the partial fulfillment of master's degree
in surgical oncology

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List of Abbreviations

3D	Three Dimensional
CM	Centimeters
CRT	Chemoirradiation
CT	Computed Tomography
CTH	Chemotherapy
CW	Chest Wall
CWR	Chest Wall Resection
DFS	Disease Free Survival
DVT	Deep Venous Thrombosis
ICU	Intensive Care Unit
IJV	Internal Jegular Vein
MFH	Malignant Fibrous Histiocytomas
MMA	Methyl Methacrylate
MRI	Magnetic Resonance Imaging
MSKCC	Memorial Sloan-Kettering Cancer Center
OS	Overall Survival
PET–CT	Positron Emission Tomography–Computed Tomography
PTFE	Polytetrafluoroethylene
RBCs	Red Blood Cells
RTH	Radiotherapy
SVC	Superior Vena Cava
TCP	Tricalcium Phosphate
WLE	Wide Local Excision

Introduction

Sternal tumors are rare tumors, they are either primary tumors (malignant tumors, benign tumors), secondary tumors (carcinoma, sarcoma), adjacent neoplasms with local invasion and non-neoplastic diseases (cysts and inflammations) **(Martini N et al., 1996).**

Sternal tumors should be considered malignant till proved otherwise. Wide resection with tumor-free margins is required in order to provide the best chance for cure in both benign and malignant lesions **(Marullia G et al., 2014).** Surgical resection of malignant sternal tumors, followed by anterior chest wall (CW) reconstruction, is associated with favorable long-term overall survival (OS) and oncological outcomes **(Chapelier A et al., 2004).**

The primary goals of anterior CW reconstruction are to prevent early and late complications. Early as postoperative ventilation problems as flail chest, protect underlying mediastinal structures and avoid CW deformity without excessive rigidity **(Marullia G et al., 2014).** Anterior CW reconstruction has been most frequently performed with non-absorbable materials, which are non-rigid and/or rigid, accompanied by soft tissue coverage **(Berthet JP et al., 2012)**. The optimal material for anterior CW reconstruction remains controversial.

Aim of the work

The aim of this study was to highlight the clinical presentation and the diagnostic work up of patients with sternal tumors, with emphasis on the outcome of surgical management and evaluate different prognostic factors.

Review of literature

Anatomy

The thoracic cage includes the sternum, the ribs and the vertebrae. The sternum consists of the manubrium, the body, and the xiphoid process the first seven pairs of ribs are the true ribs, and the last five the false ribs; of the last, ribs 8 to 10 articulate by their costal cartilages to seventh costal cartilage which is attached to sternum , while ribs 11 and 12 do not articulate at all (floating ribs). Occasionally, the 12th rib is missing **(Keith LM and Robert F, 1999).** The sternum is 15–20 cm long. The sternum serves to secure intrathoracic organs (figure 1).

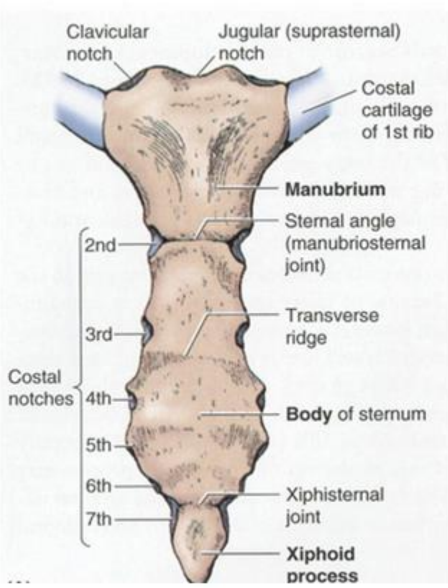

Figure 1. Anatomy of sternum

(Keith LM and Robert F, 1999).

The superior border lies in the same horizontal level as the inferior border of the body of the second thoracic vertebra **(Wilson and Herbert H. Srebnik, 2002).**

The angle of Louis, that is the Junction of the manubrium with the body of the sternum, lies on the same horizontal level with the fourth thoracic vertebra, the arch of the aorta (one vertebra higher in the infant), the beginning and the end of the aortic arch, the site where the pleural sacs meet, It marks the plane of separation of superior and inferior mediastinum, Trachea divides into 2 principle bronchi, Azygous vein arches over the roof of the Rt. Lung and opens in superior vena cava (SVC), Pulmonary trunk divides into 2 pulmonary arteries below this level, Thoracic duct crosses from right to left side and reaches left side at the level of sternal angle and It marks the upper limit of the base of the heart. The angle of Louis is useful for counting the ribs, because the second rib lies opposite to it. The xiphisternal junction lies at the level of the disk between 9th and 10th thoracic vertebra **(Petros M et al., 2012).**

Incidence

Most sternal tumors are metastatic. In particular, primary malignant sternal tumors are rare, and account for only 0.5–1.0% of all primary bone tumors. The most common primary malignant sternal tumor is chondrosarcoma, whereas osteosarcoma of the sternum is less frequent. Secondary sternal masses are more common than primary tumors. Primary sternal tumors are uncommon: benign lesions are very rare and most sternal tumors are malignant, mostly sarcomas, arising either from the bone or soft tissues of the sternum **(Martini N et al., 1996, Incarbone M et al., 1997 and Chapelier A et al., 2004).**

a) Benign sternal masses:

Osteochondromas are the most common benign tumors of cartilage and bone, occur most frequently in the ribs at the costochondral junction. Pain, bony erosion, irregular calcification, and thickening of a cartilaginous cap more than 2 cm raise the suspicion of a malignant transformation to chondrosarcoma.

Eosinophilic granuloma, a benign destructive bone lesion of unknown etiology, frequently involves the sternum. Its typical appearance is a lytic defect with well-defined margins.

Hemangiomas presenting as expansile lesions with internal trabeculations and an intact cortical margin also may involve the sternum.

Enchondromas are benign bone lesions that typically are well-defined, lobulated, and expansible lesions containing diffuse, stippled, or cartilage matrix calcification **(Stelzer P and Gay WA Jr, 1980)**.

b) Primary malignant sternal masses:

Primary malignant sternal tumors are rare entities. Chondrosarcoma is the most common primary sternal tumor **(Martini N et al., 1996).** Malignant Fibrous Histiocytomas (MFH) usually results from radiation scar. Effective treatment modality is surgical resection with wide margins. Radiation-induced MFH is rare and its treatment regards experience **(Cakir O, 2005).**

Tumors such as lung and breast carcinoma, thymoma, lymphoma, and mesothelioma also may involve the sternum by direct extension. In addition, almost any primary malignancy can produce haematogenous metastases that may involve the sternum. Although patients frequently present with a painful or palpable mass on the sternum, some are asymptomatic and the tumor is found incidentally **(Pairolero PC and Arnold PG, 1985).**

Fifteen percent of chondrosarcomas are located in the thoracic cage, making it to the most frequent primary malignant CW tumor with an annual incidence of less than 0.5 per million **(Burt M et al., 1992).**

There are few reports on chondrosarcoma of the thorax and none have been population based **(Burt M et al., 1992 and McAfee MK et al., 1985).**

Chondrosarcomas are very radio and chemo resistant. Chondrosarcoma may be conventional chondrosarcoma, clear cell chondrosarcoma, myxoid chondrosarcoma, mesenchymal chondrosarcoma or dedifferentiated chondrosarcoma. Wide Local Excision (WLE) is the therapy of choice. A complete sternectomy with corresponding resection of bilateral costal arches is performed for tumors originating in the sternum. Factors affecting prognosis include the tumor’s grade, size, and location. In the Memorial Sloan-Kettering Cancer Center (MSKCC) series, the 5-year survival for patients undergoing sternal resection for chondrosarcoma was 80% **(Martini N et al., 1996).**

In the Mayo Clinic series, 10-year survival rates were 96 % with WLE, 65 % with local excision, and 14 % with palliative excision. The other common histologies of primary malignant tumors of the sternum are osteosarcoma, plasmacytoma, and lymphoma. **(McAfee MK et al., 1985).**

c) Secondary malignant sternal masses:

Secondary sternal masses more common than primary tumors .The secondary CW masses of surgical interest arise as direct extensions of a malignancy in a contiguous organ. The breast and the lung are the most common primary sites. The initial evaluation focuses on the underlying disease, not the CW mass. For example, a patient with a CW mass resulting from direct invasion by a primary lung cancer should undergo a staging workup to determine the extent of the disease. If the patient is a stage-appropriate candidate for resection and is medically fit for surgery, he or she should undergo pulmonary resection with en bloc CWR **(Burkhart HM et al., 2002).**

Metastatic tumors involving the sternum usually originate from carcinomas of the breast, thyroid, or kidney. Although most patients cannot be cured by surgical resection, it is undertaken in some cases to palliate pain or infection of the overlying soft tissue and skin.

There is limited data available on sternal resection of non-breast secondary tumors **(Briccoli A et al., 2002)**.

Unfortunately, most women who present with a CW mass arising from a breast neoplasm have a Local Recurrence. From a technical standpoint, resection with reconstruction is feasible in this setting; however, it is unclear whether it offers any real benefit. In a study from the MSKCC, 38 women underwent extensive CWR for recurrent breast cancer. Currently, CWR for locally recurrent breast cancer must be considered on a case-by-case basis **(Downey RJ et al., 2000).**

Sternal involvement in patients with breast cancer is relatively uncommon the incidences in literature range from 1.9% to 5.2% **(Kwai AH et al., 1988; Ohtake E et al., 1994 and Lee L et al., 2008).**

Nowadays, the treatment of haematogenous solitary sternal metastases or direct local sternal/parasternal invasion breast cancer is still controversial **(Lee L et al., 2008 and Noble J et al., 2010).**

Sternal and parasternal recurrence from breast cancer can occur as result of direct spread from involved internal mammary nodes or isolated intra manubrial bone metastases with no nodal disease. Treatment historically has been with radiotherapy (RTH) as resections involve major surgery usually lasting several hours and with the potential for significant morbidity. As surgical techniques have improved resection has become a more feasible option with low associated mortality and morbidity **(Chang RR et al., 2004; Hameed A et al., 2008 and Losken A et al., 2004).**

Sternal or parasternal resection is often carried out in the palliative setting to relieve pain, odor or to remove a distressing, fungating tumor. It can also be performed where local recurrence is isolated, with the aim of achieving prolonged local control and lengthening survival in carefully selected patients. Tumors metastatic to the manubrium and the sternoclavicular area in particular, present a significant technical challenge due to their proximity to the vascular structures of the thoracic inlet and the superior mediastinum, but can be successfully resected using surgical techniques developed for the management of Pancoast tumors of the lung **(Dartevelle PG et al., 1993 and Grunenwald D, Spaggiari L. 1997).**

Clinical manifestations

Patients with sternal tumors most often have pain as their initial complaint secondary to periosteal damage or expansion. Rapidly expanding lesions more often produce pain and favor a malignant diagnosis. The character of the pain is a persistent, dull aching sensation that is likely related to stretching of the pericostal sheath.

Constitutional complaints such as fever and malaise may accompany Ewing's sarcoma. Rarely, a benign bony lesion such as osteomyelitis or eosinophilic granuloma may present as a painful bony mass with fever and malaise. Other clinical signs and symptoms produced by CW and sternal malignancies are related to invasion or pressure effects that the tumor exerts on adjacent structures **(Elizabeth AD and Blair MM, 2011).**

Radiological investigations

Careful radiological investigation is necessary to assess the extent of the tumor, as the mass evident on examination is often part of a much larger tumor invading the sternum. Computed Tomography (CT) scans have become the mainstay of imaging to evaluate the extent of the tumor and search for pulmonary metastases, three dimensional CT has diagnostic and help in manufacturing the suitable prosthesis (figure 2). 3D CT scan used to create a model by printing it using a 3D printer. Then used for fabrication of prosthetic material **(Slobodan M et al., 2013).**

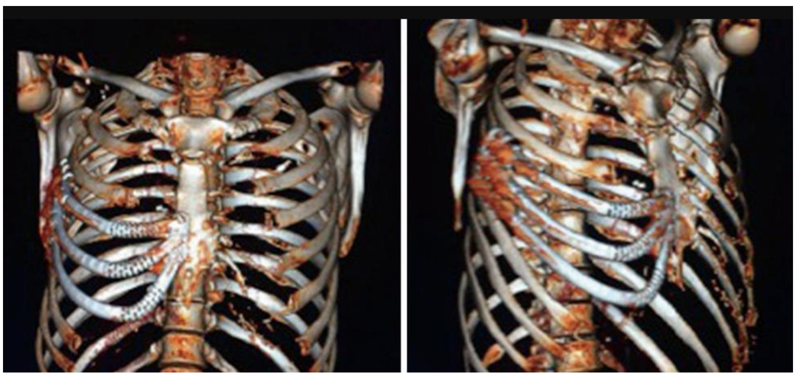

Figure 2. Three Dimensional (3D) Computed Tomography (CT) of sternum reconstructed with 3D titanium-printed implant.

(Javier A, Itzell PM, 2016).

Magnetic Resonance Imaging (MRI) has important role in evaluating sternum which is affected by neoplastic lesions, their anatomical relationships and morphological and functional characteristics may be determined along the several phases of the cancer management, either at the diagnosis, biopsy guidance , loco regional staging, clinical therapeutic, surgical or RTH planning , in the therapeutic response evaluation , or in the post-therapy follow-up. Advantages of MRI include its ability to differentiate between vascular, solid, and fluid elements in a given mass **(Padhani AR and Koh DM, 2011).**

Magnetic Resonance Imaging (MRI) is more sensitive than other modalities in detecting sternal lesions, when a lesion is indeterminate or shows signs of aggressiveness, MRI is indicated for further characterization, it can extend the diagnostic evaluation by demonstrating components such as cartilage, vascular tissue, fat and liquid. Even when a specific diagnosis cannot be made, MRI can help by narrowing the differential diagnosis. Faint lytic/sclerotic bone lesions can be difficult to visualise using only radiographs. MRI is superior to the other imaging modalities in detecting bone marrow lesions **(Ojala R et al., 2002).** Pulmonary function testing is important in patients with chronic obstructive pulmonary disease, in the elderly and in patients needing wider resection, as this will have a bearing on the postoperative CW mechanics and respiratory function **(Schaefer AR et al., 2015).**

Computed Tomography (CT) scan chest and abdomen, Positron Emission Tomography-Computed Tomography (PET-CT) and Bone scan are valuable also in detecting metastases as a preoperative routine metastatic screening **(Stark P, 1987).**

Biopsy

A preoperative tissue diagnosis should be obtained. As a general role a core-needle biopsy or an incisional biopsy needed. Both techniques provide tissue for histologic evaluation, and both must be performed in such a way that the biopsy tract will be completely excised at the time of definitive surgical treatment. As a rule, in patients with a known primary malignancy and a secondary CW mass, perform true cut or incisional biopsy **(Gattuso P et al., 1996).**

Histological analysis of a fine needle aspirate from sternal mass effective only in diagnosis of recurrence of a malignant sternal tumor.

Establishing a histological diagnosis is important and this is performed by a core needle biopsy or an incisional biopsy, however, it should be borne in mind to place the biopsy in a site where it will be excised during the surgery. Surgery is now considered the best therapeutic choice in most cases of primary sternal tumors **(Martini N et al., 1996).**

Sternal resection and reconstruction

Sternal resections and reconstructions have long been a challenge for surgeons, due to the difficulty in making full-thickness resections without compromising the stability and reconstruction of the thoracic wall, but improvements in surgical techniques now make it possible to perform even total sternectomies with good results **(Lequaglie C et al., 2002; Incarbone M et al., 1997 and Martini N et al., 1996).**

A. Sternal resection:

Chest Wall resection (CWR) is performed for a variety of conditions such as primary and secondary tumors of the CW or the sternum, lung cancer, infections, radio-necrosis and trauma **(Arnold PG and Pairolero PC. 1996).**

Sternectomy types includes total sternectomy , subtotal sternal resection in which more than 50% resected , and partial resection in which less than 50% of the sternum resected **(Incarbone M et al., 1997).**

CWR involves resection of the ribs, sternum, costal cartilages and the accompanying soft tissues and the reconstruction strategy depends on the site and extent of the resected CW defect**.**

A vertical elliptical incision is made over the sternum, extending from the sternal notch to 3-4 cm below the xiphoid process. The incision should be oriented so it encompasses any prior biopsy site of skin and soft tissues. In general, the skin and soft tissues overlying the sternum are not involved in primary or metastatic sternal tumors and can be preserved. Skin and greater pectoral muscle flaps are raised laterally for 5-6 cm from the lateral borders of the sternum if they are uninvolved by tumor (figure 3) **(Sabanathan S et al., 1997)**.

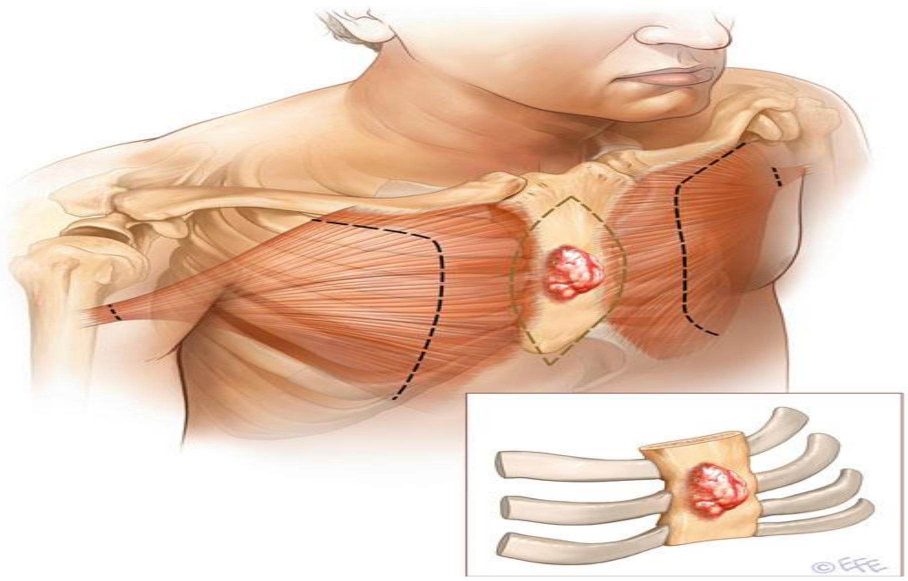

Figure 3. Sternectomy with bilateral ribs resection.

(Robert KS, 2015).

The sternal notch is dissected free, and the retrosternal space is developed. Inferiorly, the xiphoid process is excised, except in cases in which the xiphoid will be spared. The sub-xiphoid space also is developed, allowing digital palpation of the retrosternal space. The pleural reflections and diaphragmatic attachments are swept laterally. The costal cartilages on each side of the sternum are then exposed and the perichondrium is removed with a periosteal elevator. The posterior perichondrium is cut sharply to separate it from the sternum. Dissection and division of the ribs at the costochondral cartilages are advanced cephalad to the junction of the body and manubrium or extended into the manubrium itself. Once both internal mammary arteries have been ligated and both sides of the sternum have been cleared of the costochondral cartilages, a Gigli saw is used to transect the sternum **(Robert KS, 2015).**

The extent of resection for sternal tumors includes resection of the affected part of the sternum and approximately 2–3 cm of costochondral cartilage bilaterally. Usually, both internal mammary arteries are sacrificed. If a total sternectomy is performed for large tumors, the resection includes the inner third of both clavicles as well. The clavicular heads are disarticulated, and the first costal cartilage on each side is incised. In the case of smaller tumors involving the sternal body only, it often is possible and desirable to preserve the manubrium. If this is undertaken, the body of the sternum is disarticulated from the manubrium **(Pairolero PC and Arnold PG, 1985).**

Preferentially, we prefer a minimal 2 cm. margin developed 360 degrees around the periphery of the planned resection area margins should extend a minimal one intercostal space above and below the tumor mass inclusive of the cephalad caudad aspect of the planned rib resections **(Martini N et al., 1996 and McAfee MK et al., 1985).**

Partial or total sternectomy associated or not with the resection of other related surrounding tissues is the technique of choice to obtain a safety margin and the radical treatment of the disease **(Lee L et al., 2008; Noble J et al., 2010; Nakamura H et al., 2007 and Lequaglie C et al., 2002).**

B. Sternal reconstruction:

CW reconstruction has been a complex problem in the past due to intraoperative technical difficulties, surgical complications, and respiratory failure caused by the CW instability and paradoxical respiratory movements **(Pairolero PC, Arnold PG 1985 and Sabanathan S et al., 1997).**

The most challenging part is the reconstruction of the anterior CW in order to prevent respiratory insufficiency, local infection, injuries to mediastinal structures, functional and cosmetic results. The literature reports various techniques using different materials for sternochondral reconstruction **(Noble J et al., 2010; Nakamura H et al., 2007; Lequaglie C et al., 2002 and Chapelier AR et al., 2004).**

If the defect is small then a synthetic mesh is used to cover the defect with soft tissue over it. However, if the defect is large then a composite prosthesis is created with methyl methacrylate (MMA) and Marlex or Polytetrafluoroethylene (PTFE) mesh to avoid paradox and ensure protection of intra-thoracic organs often in combination with soft tissue reconstruction using a variety of myocutaneous flaps **(Deschamps C et al., 1999; Novoa N et al., 2005 and Weyant MJ et al., 2006).**

Various prostheses are available for reconstruction of sternum and anterior CW **(McCormack PM, 1989 and Mansour KA et al., 2002).**

Advances in the fields of surgery and anesthesia and the team effort of the involved thoracic and plastic surgeons result in more aggressive resections. Nowadays neither the size nor the position of the CW defect limits surgical management, because resection and reconstruction are performed in a single operation that provides immediate CW stability **(Arnold PG and Pairolero PC, 1996).**

Numerous time-honored materials and techniques have been extensively described and still provide the basis for adequate functional restoration following sternectomy. The thoracic surgeons' decision of how to reconstruct CW and sternal defects must take into account the patient's age, extent of resection, defect size, and presence of infection or prior radiation **(Bille A et al., 2012 and Shen K, 2015).**

I. Mesh Materials And Patches:

a) Polytetrafluoroethylene (PTFE) implants

Polytetrafluoroethylene (PTFE) implants are made of a non-biodegradable fluorocarbon synthetic polymer **(Wikipedia et al., 2014).**

b) polypropylene mesh:

Resection that extends beyond four ribs will routinely require rigid CW reconstruction. This maneuver constitutes the creation of mesh with polypropylene that may be used as a singular sheet or with creation of a mesh (sandwiched) together with MMA.

Myocutaneous flaps should be liberally used to cover these reconstructions. When defects are small and there is less probability for creation of flail chest, mesh alone may be sufficient with this smaller area for coverage **(PromHoward JH et al., 2010).**

It is easy to handle, shape, and fix into the surrounding ribs. It also has a high tensile strength that can provide the rigid support needed to stabilize the CW and prevent respiratory compromise. In vivo, its high biocompatibility (inertness) helps decrease the inflammatory reaction and adhesions formation with the underlying viscera **(Brown GL et al., 1985; Pairolero PC, Arnold PG, 1985 and Gore et al., 2015).**

Despite being rigid enough to protect against paradoxical movement of the chest wall, sometimes the strength of these patches may not be sufficient to protect against external trauma, especially when used for anterior CW reconstruction, even when tightly stretched over the defect area **(Thomas PA and Brouchet L, 2010).**

Therefore, these patches are often reported in combination with other rigid prosthesis like titanium bars **(Nagayasu T et al., 2010; Sunil L et al., 2006 and Hamad AM et al., 2009).**

c) Biological Meshes and Patches:

Biological Meshes and Patches the most commonly used biological Acellular Dermal Matrices are either human derived, porcine derived or bovine derived **(Holton LH et al., 2007).**

II. Rigid and Semi-rigid Prostheses:

a) **Bone Allografts and Xenografts:**

The unique properties of bone graft material make it an ideal choice for sternal defect reconstruction **(Finkemeier CG, 2002 and Khan SN et al., 2005).**

Tissue banks provide a potential unlimited source of allografts, making them readily available for medical use. They are ideal for use in large full thickness sternal defects, where the use of autografts would have led to additional cosmetic and functional impairment in the donor site **(Marulli G et al., 2010; Stella F et al., 2012 and Myeroff C, Archdeacon M, 2011).** Recently, some authors have used bone allografts (usually fixed to the thoracic wall using titanium devices) to replace the sternum (figure 4).

Figure 4. Sternal reconstruction using bone allograft fixed to the surrounding ribs with titanium plates

(Marulli G et al., 2010).

Until now, no rejection or infection related to the use of allograft has been reported during the follow-up period, confirming the biocompatibility of these grafts **(Rocco G. 2010; Marulli G et al., 2010 and Stella F et al., 2012).**

b) Titanium Prosthesis:

Traditionally, plates and screws were used for sternal reconstruction as transverse bridges fixed to the ribs on both sides **(Luh SP et al., 1996).** More recently, two sternal fixation systems originally designed for sternal stabilization after postoperative Mediastinitis and sternal dehiscence were used successfully in reconstructing sternal defects (Synthes and LeyTM prosthesis) **(Bille A et al., 2012; Fabre D et al., 2012 and Voss B et al., 2007).**

The Synthes sternal fixation system is much like the traditional titanium plates but specifically made to fit into the geometrical configuration of the anterior CW (figure 5) **(Hamad AM et al., 2009; Voss B et al., 2007 and Lee TY et al., 2007).**

Figure 5. Sternal reconstruction using Synthes

(Huh J et al., 2008).

Another titanium rigid system consisting of titanium bars and rib clips (STRATOSTM) is now gaining popularity for CW reconstruction with some reports showing its efficacy in sternal reconstruction. The rib clips make its application much easier without the need to use drilling machines or screws (figure 6) **(Bille A et al., 2012; Mathes SJ. 1995; Fabre D et al., 2012; Berthet JP et al., 2012; Corcoles JM et al., 2014 and Huh J et al., 2008).**

Figure 6. The use of STRATOSTM bars to reconstruct anterior CW defect

(Westphal FL et al., 2014).

Three-Dimensional (3D) custom made titanium neo sternum (ThoRibTM) used in the reconstruction of anterior CW defect. The neo sternum, designed based on the preoperative CT images. The prosthesis has more strength than simple bars, and thus it is more protective while providing excellent cosmetic outcome (figure 7) **(Demondion P et al., 2014).**

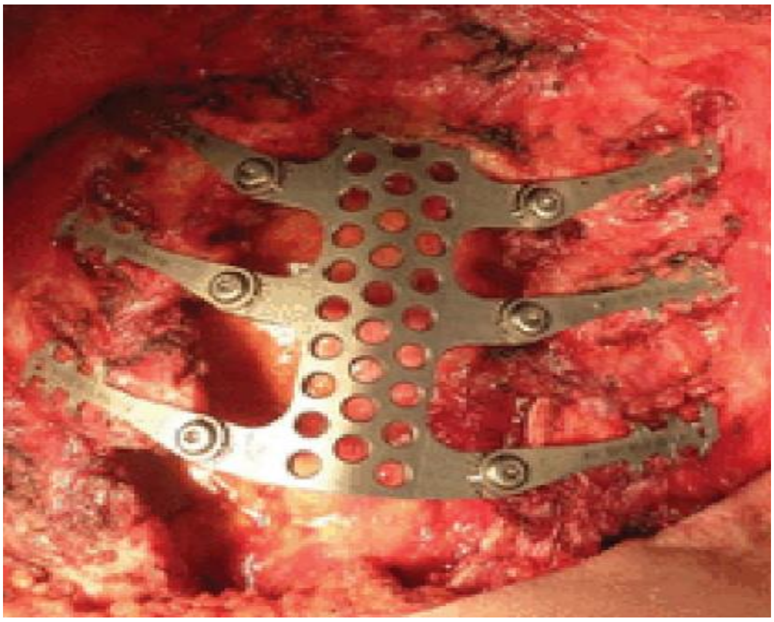

Figure 7. Custom-made Titanium neo-sternum (ThoRib™) fixed in place using rib clips

(Demondion P et al., 2014).

Titanium mesh (widely used for cranial reconstruction) can also be used to reconstruct sternal defects. They are rigid enough to provide the stability needed to avoid respiratory compromise. Also, they are easy to shape and apply and can be used without additional autologous soft tissue coverage **(Ersoz E et al., 2014 and Rong G, Kang H. 2013).**

Titanium prostheses have several advantages; they are inert and resist corrosion and biochemical degradation, have the highest strength for weight ratio of any metal, have the ability to integrate into nearby bony structures, and do not interfere with imaging techniques **(Horio H et al., 2005).**

c) Calcium Ceramics:

The most common clinically used bioceramics are hydroxyapatite, Tricalcium Phosphate (TCP), and calcium phosphate bone cements. **(Breitbart AS et al., 1995 and Breibart AS et al., 2013).**

A hydroxyapatite TCP bioceramic prosthesis used for sternal defect reconstruction (figure 8) **(Watanabe A et al., 2003).**

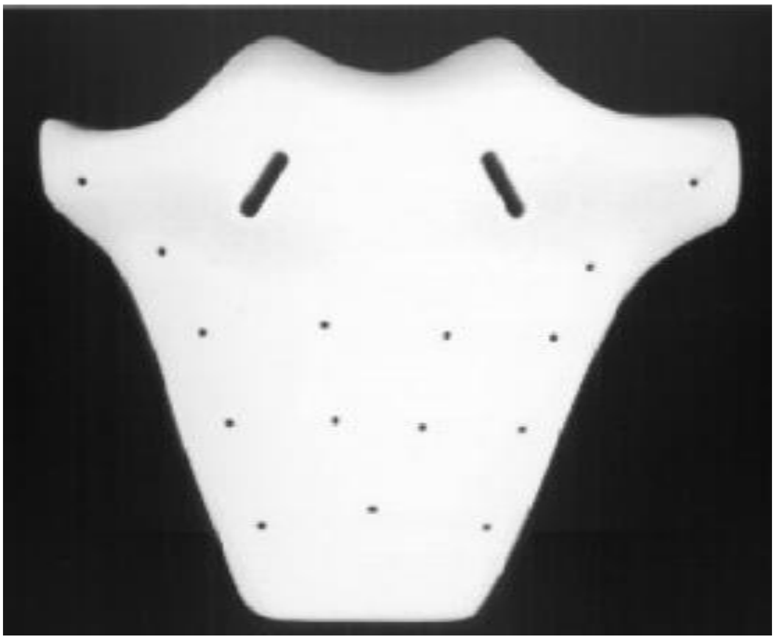

Figure 8. Calcium ceramic neo-sternum

(Watanabe A et al., 2003).

They mentioned that the biomechanical characteristics of this prosthesis help resist infection and restore the functional and morphological characteristics of the original sternum. The main drawback of bioceramics is their low compressibility, making them liable to breaking or shattering on exposure to high force external trauma. Also, it is rather difficult to fix them into position, and their elevated costs may prevent a more widespread future clinical use **(Watanabe A et al., 2003).**

d) Three-Dimensional (3D) Printed Prosthesis:

Three-Dimensional 3D printing and casting technology used to manufacture a sternum like implant. The 3D printing material is neither suitable nor medically approved to be used as a prosthetic implant. Therefore, CT images were used to produce the neo sternum prototype by the 3D printing process. This prototype was then used to form a polyurethane foam casting mold, which was later filled with the MMA bone cement to produce the final neo-sternum implant. After proper sterilization, the prosthesis was then fixed to the surroundings using K wires (figure 9). **(Stojkovic M et al., 2010 and Milisavljevic S et al., 2013).**

Figure 9. Prothesis made through 3D printing used for sternal reconstruction

(Stojkovic M et al., 2010).

e) Biodegradable Polymers:

The biocompatibility and biodegradability of these prosthesis makes them ideal for use in cases of bacterial contamination of the operative fields and in growing children. They can be shaped easily with sharp or heating instruments, provide reasonable rigidity to stabilize the anterior chest wall, preserve their strength for a long period after the operation, and do not require be removing or replacing in cases of infection. After being completely resorbed, the resultant fibrous tissue is strong enough to protect the intrathoracic organs and prevent paradoxical CW movement **(Tuggle DW et al., 2004).**

Miller et al. reported the use of poly-lactic acid bar (BioBridge) in CW and sternal reconstruction (figure 10).

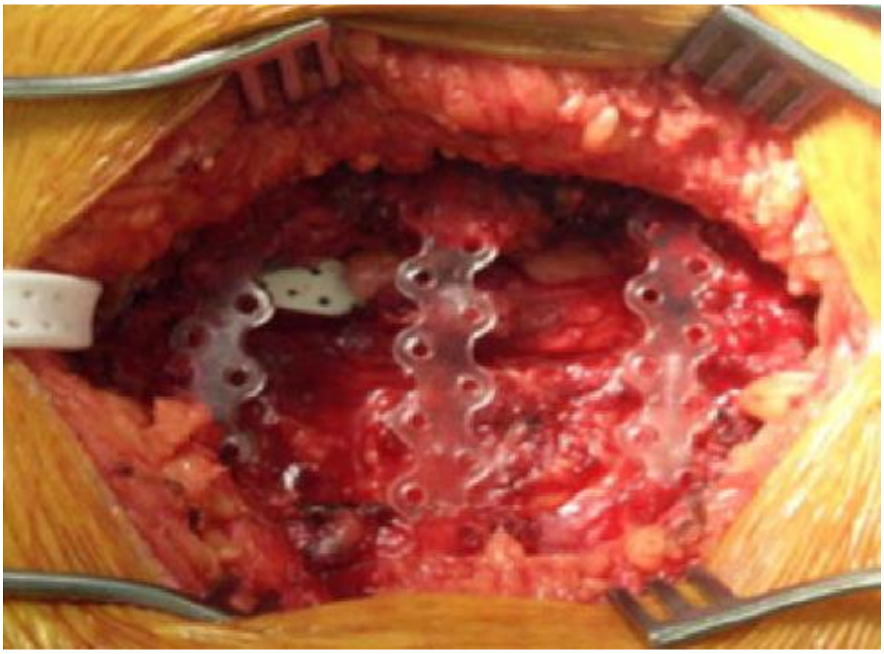

Figure 10. BioBridge bars used for CW reconstruction

(Miller DL et al., 2013)

They mentioned that it can be used in small to moderate sternal defects but not in large ones due to the higher risk of paradoxical movement with subsequent respiratory impairment **(Miller DL et al., 2013).**

Tuggle et al. used the LactoSorb plate (copolymer consisting of 82% L-Lactic acid and 18 % glycolic acid) for anterior CW reconstruction in four children and reported no postoperative morbidities (figure 11).

Figure 11. Lactosorb plate used for sternal reconstruction in a child

(Tuggle DW et al., 2004).

f) Nanocomposites:

The recent advances in nanotechnology have led to the experimental use of the biodegradable nanocomposite prosthesis as a valid alternative in bony defect reconstruction **(Loher S et al., 2006; Buschmann J et al., 2012; Rezwan K et al., 2006 and Schneider OD et al., 2008).**

g) Bioengineered Stem Cell Derived Bone Grafts:

In the long lasting journey toward the production of human spare parts using bioengineered stem cells, major advances in the past years have led to the creation of human like bone that can be used as bone grafts. In this process, the amniotic or mesenchymal stem cells are incorporated into a biocompatible degradable scaffold materials (copolymers, bioactive glasses, and ceramics) allowing for the subsequent bone growth, while the scaffold is being slowly resorbed **(Schubert T et al., 2013; Steigman SA et al., 2009; Klein JD et al., 2010; Mano JF, Reis R. 2007; Bernhardt A et al., 2008; Mastrogiacomo M et al., 2005 and Marcacci M et al., 2007).**

Steigman et al. reported the use of bone grafts engineered from amniotic mesenchymal stem cells for sternal repair in animal models with promising results for future implementation in human patients **(Steigman SA et al., 2009).**

This technology seems to offer an ideal reconstructive material to be used for growing children due to their bone growing capabilities.

III. Soft tissue reconstruction:

a) Pectoralis major myocutaneous flap:

The double breasting technique of the pectoralis major muscle flaps with rectus sheath extension is efficient in covering the entire length of the sternectomy defect and can reduce the morbidity, without affecting the function of the shoulder joint (figure 12).

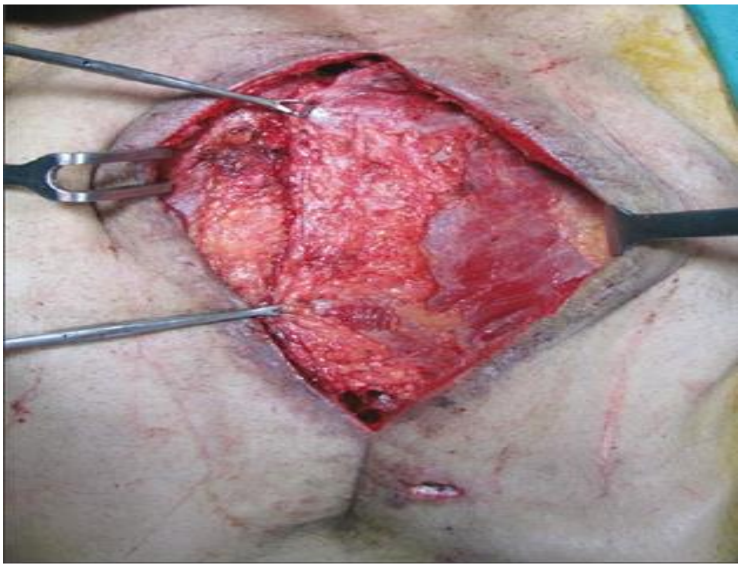

Figure 12. Bilateral pectoralis major muscle flap

(Sahasrabudhe P et al., 2011)

The pectoralis major muscle is supplied by one dominant vascular pedicle (thoracoacromial artery) and several secondary pedicles consistent with a Mathes and Nahai type V muscle flap.

Harvest Technique:

The surface markings of the muscle are easily identified with the clavicle superiorly, sternum medially, and the anterior axillary fold laterally. The pedicle originates from the axillary artery at the midpoint of the clavicle and heads inferiorly before arcing medially to follow a line drawn from the acromion process to the xiphoid.

In CW reconstruction, the pectoralis flap is most commonly used as a muscle advancement or rotation flap based on the thoracoacromial pedicle **(Karim B et al., 2011).**

b) The latissimus dorsi flap:

The latissimus dorsi flap is one of the true workhorse flaps in general reconstructive surgery. Owing to its large potential size, possibility for incorporating multiple tissue types, relatively long pedicle and robust vessels, it is arguably one of the most versatile flaps suited for chest reconstruction **(Olivari N, 1980).**

It is now commonly used for coverage of both extrathoracic defects as a musculocutaneous flap and intrathoracic defects to obliterate dead space as a muscle-only flap **(Arnold PG and Pairolero PC, 1989).**

Vascular Anatomy

The latissimus is a type V muscle, and its vascular anatomy is almost a mirror image of the pectoralis flap. The dominant pedicle is the thoracodorsal artery, a terminal branch of the subscapular artery that itself arises from the third portion of the axillary artery (**Rowsell AR et al 1984).**

Harvest Technique

Optimal positioning for latissimus dorsi (LD) flap harvesting is typically the lateral decubitus position, with the arm prepped and the shoulder flexed to 90 degrees, the latissimus is harvested in this position, and the donor site can be closed prior to repositioning the patient and insetting the flap anteriorly. The axis and length of the thoracodorsal pedicle afford this flap an excellent arc of rotation, and virtually any part the ipsilateral chest wall can be reached **(Karim B et al 2011).**

c) Omental flap:

Which designates an increase in potential morbidity as it adds complexity to the CW defect with abdominal entry the omental flap is based upon the right gastroepiploic artery that is utilized for tissue coverage, with selection of this approach the upper midline laparotomy incision is utilized for access to the omentum.

Multiple techniques have been used to correct CW defects following subtotal or total sternectomy. Indeed, the impact of a sternectomy on CW function is major, including paradoxical respiration, prolonged Intensive Care Unit (ICU) stay, prosthetic material infections and reoperation **(Mansour KA et al., 2002; Weyant MJ et al. 2006 and Chapelier A et al., 1994).**

Patients and methods

This is a retrospective study included patients with sternal tumors, who underwent sternal resection at National Cancer Institute during the last 10 years. Data of all patients will be collected from the medical record of these patients as:

- Demographic and clinic-pathological features including age, sex, clinical presentation and anatomical site.
- Radiological investigations done as CT, MRI or nuclear scanning.
- Pathological data including the type of the pathology, tumor necrosis after neoadjuvant chemotherapy and resected surgical margins.
- Surgical data as extent of the resection, reconstruction and perioperative complications.
- Survival data and recurrence rate.

Inclusion criteria:

Patients with good performance who underwent surgical resection at the surgical department at National Cancer Institute, Cairo University from January 2005 to January 2015.

- Any age.
- Any sex.
- Primary or secondary sternal tumors.
- No distant metastases otherwise the single metastasis site for which sternectomy was done.
- No associated major co-morbidities.

Statistical methods:

Data was analyzed using IBM SPSS advanced statistics version 22 (SPSS Inc., Chicago, IL). Numerical data were expressed as mean and standard deviation or median and range as appropriate. Qualitative data were expressed as frequency and percentage. Chi-square test or Fisher's exact test was used to examine the relation between qualitative variables. For not normally distributed quantitative data, comparison between two groups was done using Mann-Whitney test (non-parametric t-test). Survival analysis was done using Kaplan-Meier method and comparison between two survival curves was done using log-rank test. All tests were two-tailed. A p-value < 0.05 was considered significant.

Protection of privacy and confidentiality:

The data of the patients will be presented anonymously with protection of privacy and confidentiality.

Results

This study included 21 patients (11 males and 10 females). Mean age of our patients was 40 years old and ranged from 18 to 56 years old.

Ratio of patients more than 40 years constituted 52.4 % of patients diagnosed with sternal tumors at all age groups, ratio of patients who were less than 40 years constituted 47.6%.

Clinical presentation

a. Site of sternum incorporating the mass:

The most common site within the sternum was the upper part of the body in 13 cases (61.9%) (Table 1), nine of them was purely in the upper part, the other 4 cases the mass was incorporating the manubrium and the upper part of the sternum (figure 13).

Table 1: Site within the sternum.

Mass location within the sternum	**Frequency**	**Percent**
Manubrium	6	28.6
Upper part of body	9	42.9
Lower part of body	1	4.8
Whole sternum	1	4.8
Manubrium & upper part of body	4	19.0

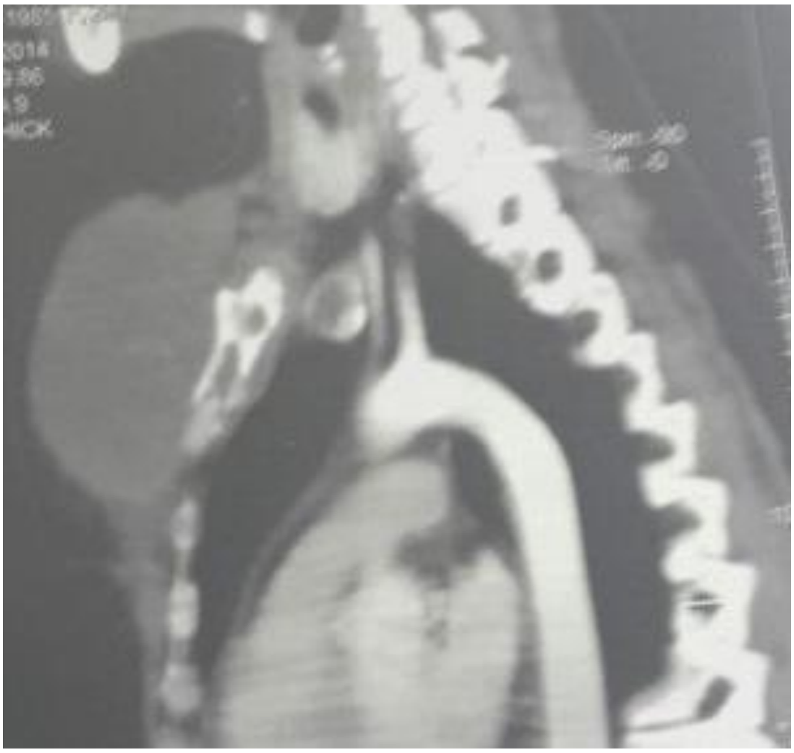

Figure 13. Chondrosarcoma in the manubrium and upper part of the sternal body CT**.**

b. Size of the mass :

The size of maximum diameter of the sternal mass clinical examination ranging from 4×3 to 22×5 cm.

Yalk sac tumor invading sternum had the largest maximum diameter 22 cm (figure 14) and his CT chest with intra venous contrast (figure 15).

Median Maximum diameter of mass was 6 cm. which in fifteen patient (71.4%) were below or equal to 6 cm as maximum mass diameter. the remaining 6 patients (28.6%) had diameter more than 6 cm.

Figure 14. Yalk sac tumor invading sternum.

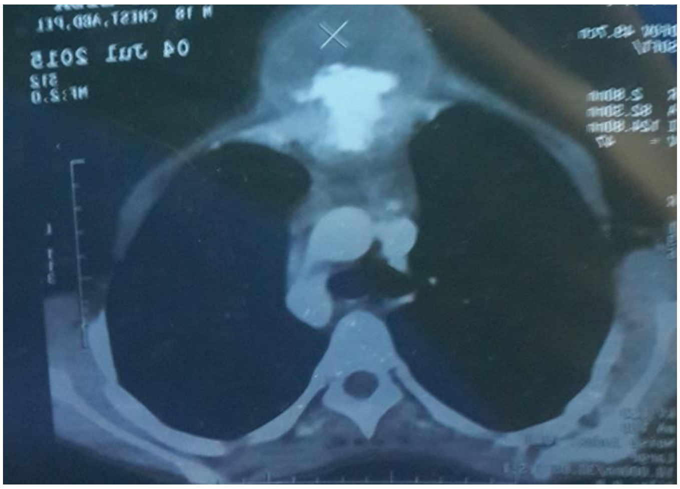

Figure 15. Yalk sac tumor invading sternum CT.

c) Preoperative biopsy:

Preoperative biopsy was inconclusive in 4 patients, for preoperative tissue diagnosis see (Table 2).

Table 2: Preoperative biopsy.

	Frequency	Percent
Chondrosarcoma	6	28.6
Duct carcinoma	4	19.0
Scanty	4	19.0
Carcinosarcoma	1	4.8
Chondroid tumor	1	4.8
Chondroma	1	4.8
Follicular thyroid carcinoma	1	4.8
Osteosarcoma	1	4.8
Transitional cell carcinoma	1	4.8
Yolk sac tumor	1	4.8

Treatment

i. Preoperative therapy:

Neoadjuvant therapy was added to 9 patients (42.9%). Five of them was recurrent breast cancer after mastectomy, four of them received CTH and RTH, the last one received CTH alone, one patient diagnosed as chondrosarcoma received preoperative therapy, another patient treated by chemoirradiation (CRT) at Sudan then referred to National Cancer Institue.

One patient previously diagnosed as Hodgkin's lymphoma which was treated since 20 years by 6 cycles CTH and 25 sessions RTH then during follow up ,splenectomy was done for relapse of Hodgkin's lymphoma since 16 years ,then he received 6 cycles CTH ,then during follow up, he was diagnosed as clavicle osteosarcoma since 2 years ,for which he received neoadjuvant 6 cycles CTH ,then surgical resection of the right clavicle with safety margin was done ,followed by 10 cycles CTH ,then follow up for another 2 years, then recurrence of osteosarcoma on manubrium for which sternectomy and resection of right 1st rib as a safety margin was done and soft tissue reconstruction by pectoralis major myocutaneous flap was done ,followed by concomitant CRT as 30 session RTH and 8 cycles of Ifosfamide and Etoposide, now this patient on follow up .

Mediastinal yolk sac tumor patient received neoadjuvant CTH, on which the mass increased denoting treatment failure.

One patient diagnosed as uterine cervical cancer treated by Wertheim operation then received CRT.

ii. Surgical resection:

1. Procedure of local resection:

Subtotal sternectomy was the most common procedure, done in 13 patients (61.9%), in which more than 50% of the sternum resected partial sternectomy done in 6 patients (28.6%) total sternectomy done only in 2 patients (9.5%).

2. Extended resection:

En-block resection of nearby structures during sternectomy was done in 11 patient (52.4%) all of them include ribs resected with or without other organs (figure 17).

Median number of resected ribs was 4 ribs ranging from 1 to 8 ribs.

Eight ribs resected in 4 patients, one rib resected in only one patient (Table 3).

Table 3: Number of resected ribs.

Number of resected ribs	**Frequency**	**Percent**
1	1	9.1
2	3	27.3
3	1	9.1
4	2	18.2
8	4	36.4

Excision of 3 ribs was done beside to sternectomy in chondrosarcoma patient (figure 16).

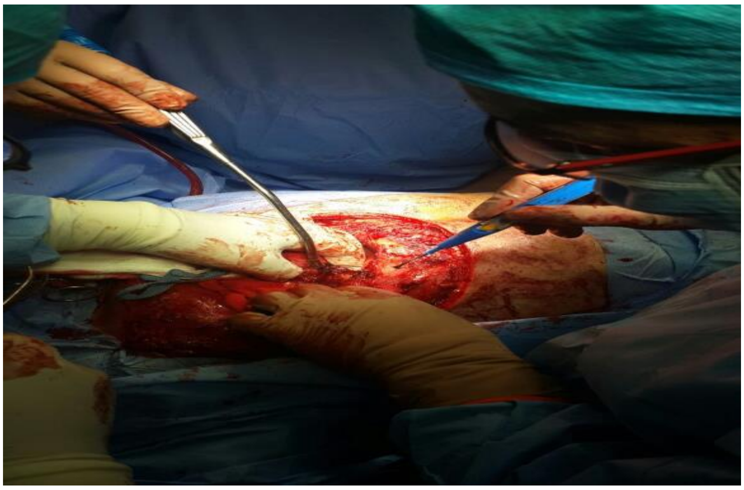

Figure 16. Resection of nearby ribs.

Seven patients have organs with ribs have been resected (63.6%). The clavicle was the commonest resected organ.

Resection of nearby organs (Rt. middle lobe, pericardial fat and piece of pericardium) done in metastatic cervical squamous cell carcinoma patient (figure 17).

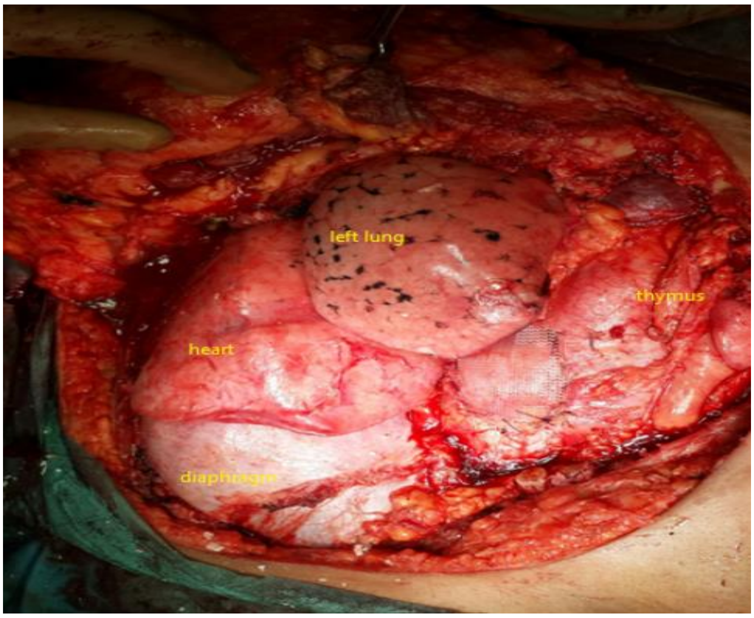

Figure 17. Resection of nearby organs done in metastatic cervical squamous cell carcinoma patient.

During sternectomy for chondrosarcoma, we found the tumor was continues with a mass inside SVC (figure 18).

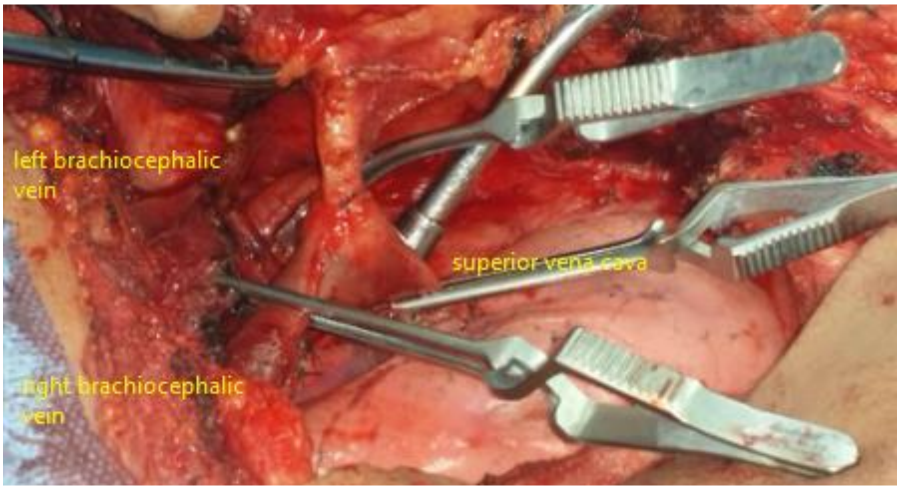

Figure 18. Mass inside the SVC in sternal chondrosarcoma patient**.**

Thrombectomy was done during excision sternal chondrosarcoma from SVC (figure 19).

Figure 19. Thrombectomy was done during excision sternal chondrosarcoma from SVC**.**

3. Defect size after resection:

Median defect size post excision was 88 cm². Ranging from 25 to 432 cm².Defect size after resection measure in cm².in 13 patients (61.9%) the defect size was smaller or equal to 100 cm².

Maximum defect size after sternectomy occurred in yalk sac tumor invading the sternum was 432 cm² (figure 20)**,** showing the specimen after resection (figure 21).

Figure 20. Maximum defect size after sternectomy occurred in yalk sac tumor invading the sternum was 432 cm^2.

Figure 21. Yalk sac tumor invading the sternum specimen.

4. Intra operative Blood transfusion:

Median Intra operative Blood transfusion was 2 units. Ranging from 1 to 5 units. Intraoperative Blood transfusion needed in 18 patients.

iii. Reconstruction:

1. Rigid reconstruction:

After resection, reconstruction by rigid reconstruction was done in 20 patients (95.2%).Polypropylene mesh was inserted for the large defect after resection of mediastinal yalk sac tumor invading the sternum (figure 22).

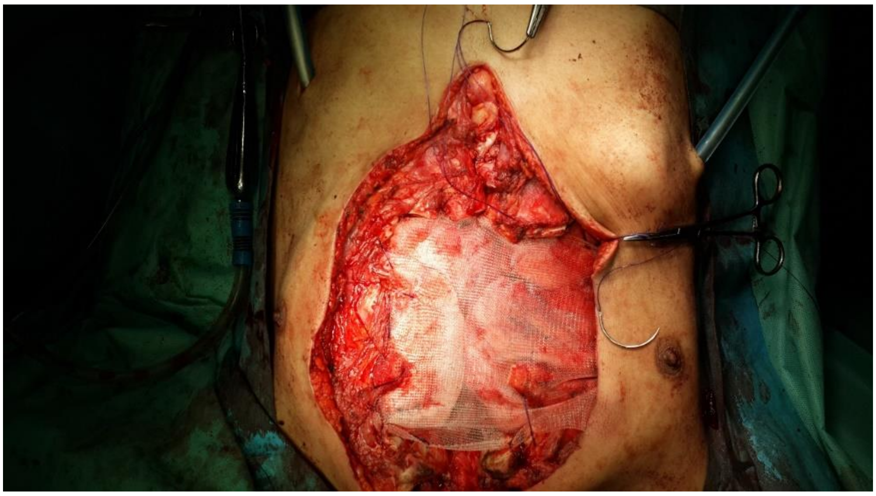

Figure 22. Polypropylene mesh for the large defect after resection of mediastinal yalk sac tumor invading the sternum.

Then processing of MMA and double polypropylene mesh in the form of “sandwich” prosthesis (figure 23).

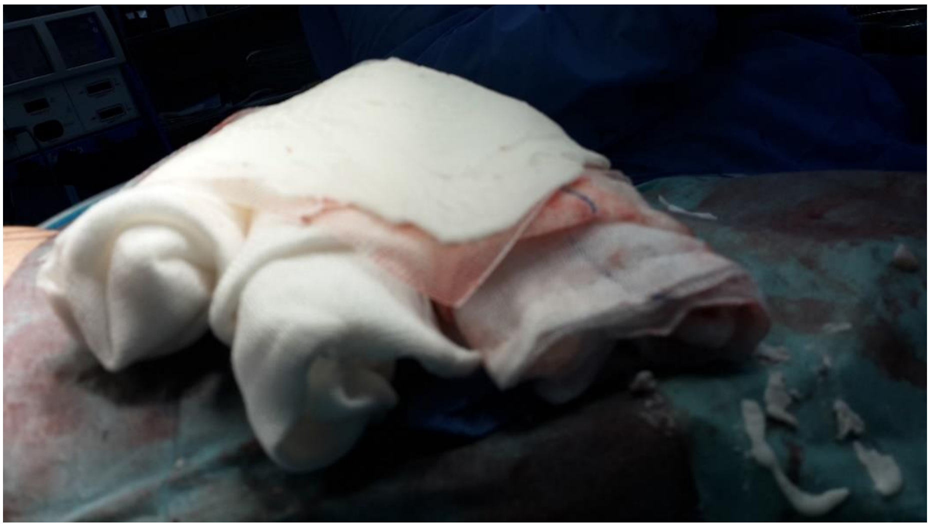

Figure 23. Methyl Methacrylate (MMA) and double polypropylene mesh processing in the form of “sandwich” prosthesis.

Then MMA and double polypropylene mesh inserted to cover the defect (figure 24).

Figure 24. Methyl Methacrylate (MMA) and double polypropylene mesh insertion to cover the defect.

Then, MMA and double polypropylene mesh fixation all around the defect (figure 25).

Figure 25. Methyl Methacrylate (MMA) and double polypropylene mesh fixation all around the defect.

2. Soft tissue reconstruction:

Then, soft tissue reconstruction was done in 14 patients (66.7%), 13 of them by pectoralis major myocutaneous flap (92.9%), only in one patient reconstruction done by omental flap (7.1%).

Additional soft tissue reconstruction as bilateral pectoralis major flap for chondrosarcoma patient (figure 26) to cover the MMA and double polypropylene mesh approximation of both pectoralis major flap together to cover the prosthesis (figure 27).

Figure 26. Bilateral pectoralis major flap as additional soft tissue reconstruction for chondrosarcoma patient.

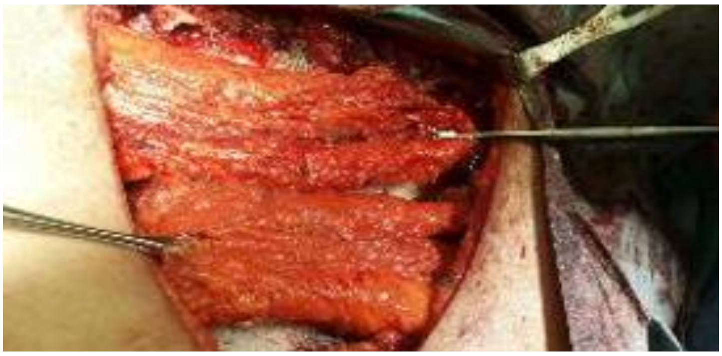

Figure 27. coverage of the MMA and double polypropylene mesh by bilateral pectoralis major muscle flap.

iv. Complications:

1. **flail chest:**

Flail chest occurred in 3 patients (14.3%). two of them needed post operative mechanical ventilation in the 1st patient 2 days needed until extubation, in the 2nd patient (yolk sac tumor) 6 days needed for extubation .

2. **Pneumonia:**

Pneumonia occurred in 4 patients (19%). two of them need mechanical ventilation.

Out of the 21 patients, four of them complicated by pneumonia, three of them occurred in patients in which subtotal sternectomy done, and the remaining one was yolk sac tumor patient in whom total sternectomy was done.

Out of the 21 patients, twenty of them had rigid reconstruction after sternectomy, 16 of the 20 patients (80%) did not complicated by pneumonia. The remaining 4 patients (20%) complicated by pneumonia osteosarcoma patient was the only one who did not need rigid reconstruction and he did not suffer from pneumonia.

3. **Other Complications:**

Complications other than respiratory complications, occurred in 7 patients (33.3%) of them, 4 patients (57.1%) complicated by local sepsis, three of them was superficial, and one patient had deep wound infection treated by removal of the cement after 4 months, one patient complicated by DVT in superior vena cava (figure 28), another one complicated by hoarseness due to intentional resection of Rt. recurrent laryngeal nerve during sternectomy for osteosarcoma the last patient died by day 10 postoperatively.

Figure 28. SVC thrombus.

Fourteen of the 21 patients had soft tissue reconstruction after sternectomy, 10 of the 14 patients (71.4%) did not complicated by local sepsis, DVT nor hoarseness . the remaining 4 patients (28.6%) had one of the following complications: local sepsis, DVT or hoarseness.

v. ICU and Hospital admission:

All patients except recurrent breast cancer needed ICU admission. Median ICU admission days were 2 days ranging from 1 to 10 days. Eight patients admitted to surgical ICU for only one day post operative seven patients admitted for 2 days in surgical ICU so, fifteen patients (75%) needed 1 day in surgical ICU, five patients (25%) needed more than 2 days in surgical ICU.

Total hospital admission was ≤ 10 days in 12 patients (57.1%). Median hospital stay days were 10 ranging from 6 to 25 days hospital admission was 25 days in 2 patients least hospital stay occurred in 3 patients was 6 days.

vi. Pathology:

1. **Final pathological diagnosis:**

Chondrosarcoma was the most common type of sternal tumors in the 21 patients by 8 patients (38.1%).

The 2^{nd} most common type was recurrent breast cancer by 5 patients (23.8%) (figure 29).

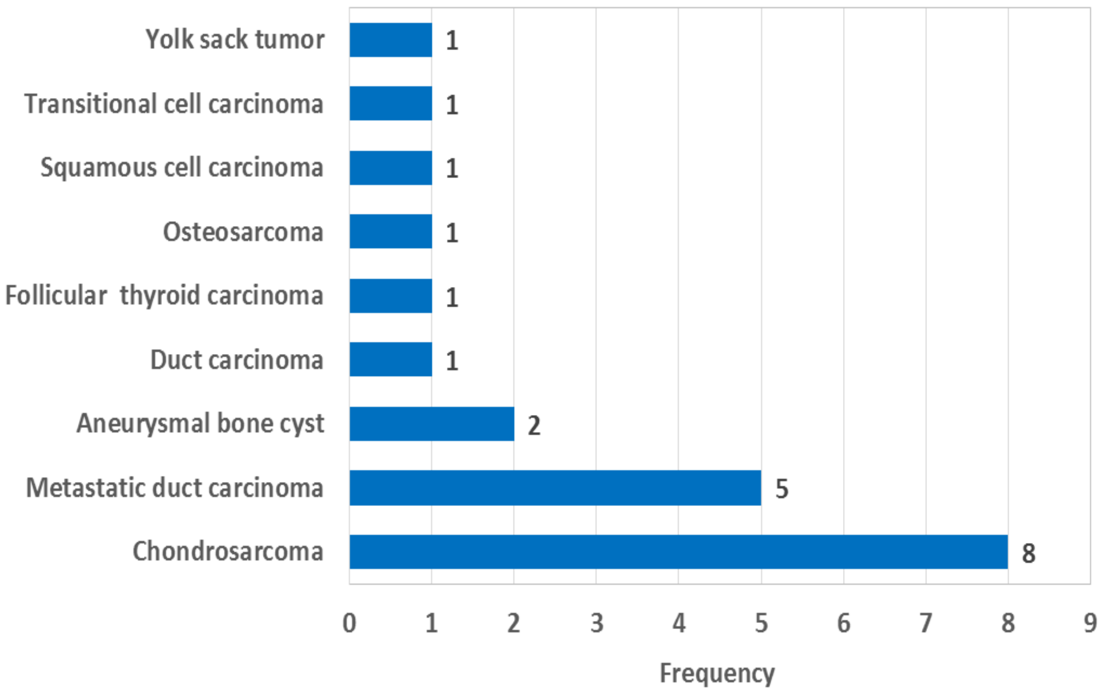

Figure 29. Final pathological diagnosis.

Sternal masses resected in this study were benign in 2 patients (9.5%) and malignant in 19 patients (90.5%), eleven of them were secondary tumors (57.9%), the remaining 8 were primary tumors (42.1%).

2. **Surgical margin:**

Negative margin was found in 16 patients, the remaining 3 patients had positive margin.

3. **Grade:**

Out of 19 malignant masses, ten of them (52.6%) were high grade. the remaining 9 patients (47.4%) were low grade.

vii. Adjuvant therapy:

Two patients received adjuvant therapy, one of them received adjuvant CTH post resection of osteosarcoma and Metastatic follicular thyroid cancer patient received adjuvant radioactive iodine therapy.

Survival

Median Follow up time was 31 months. Ranged from 2 to 124 months.

Fourteen out of the 21 patient (66.7%) still alive during follow up visits two out of 21 patients excluded from calculating OS and DFS as they were diagnosed as benign lesions. Nineteen patients out of 21 diagnosed as a malignant lesion, so we have statistically studied them by OS in relation to different prognostic factors.

Recurrence occur after resection in 2 patients (9.5%). One of them was recurrent breast cancer suffered from Local Recurrence after 6 months which was treated with re surgery, the other one diagnosed as chondrosarcoma had local and systemic recurrence after 2 months.

We found that one year OS was 89.5 %, 2 and 3-year OS was, were 76.9 % and 69.2% respectively.

We found that one year DFS was 84.2 %, two year DFS was 72%, and 3-year DFS for the 19 patient who diagnosed to had malignant disease to be 64.8%.

Three year OS was 88.9% regarding male patients and 49.2% regarding female patients (figure 30). The relation between gender and OS showed a statistical significance (p value 0.051).

Three year DFS was 88.9% regarding male patients and 49.2% regarding female patients (figure 31). The relation between gender and DFS showed a statistical significance (p value 0.029).

This difference explained by increased incidence of recurrent breast cancer patients in females.

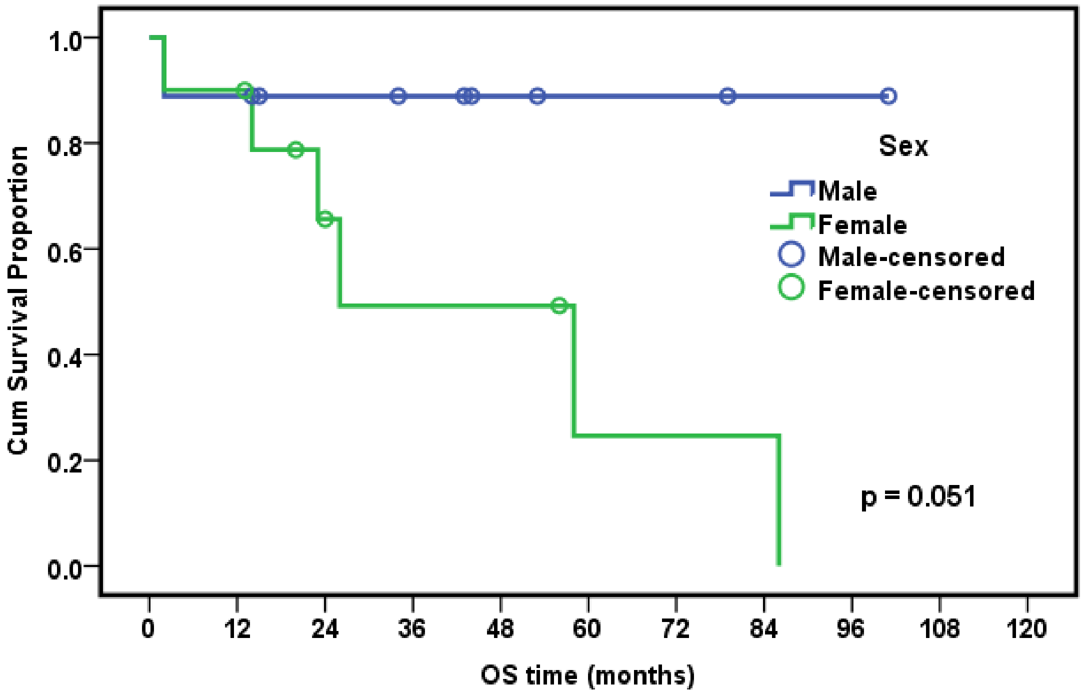

Figure 30. Overall Survival (OS) and its relation to gender as a prognostic factor.

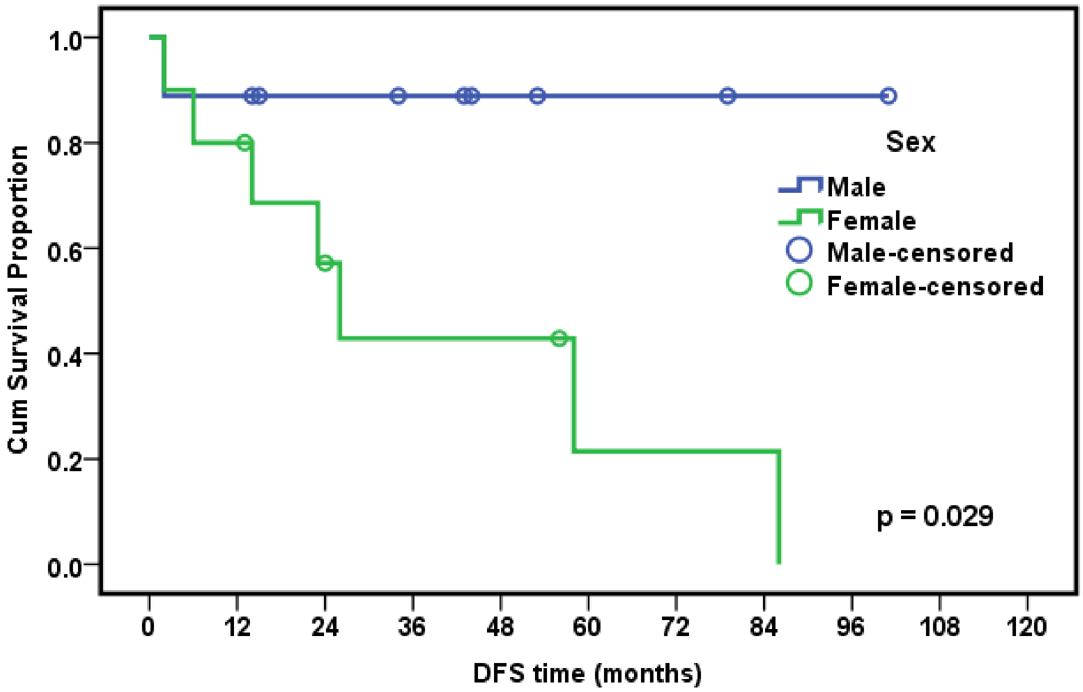

Figure 31. Disease Free Survival (DFS) and its relation to gender as a prognostic factor.

Primary tumors group 3-year OS was 87.5% (figure 32), and secondary tumors group 3-year OS was 50.5%, so we found no significant difference in OS in both groups (p value 0.465).

Primary tumors group 3-year DFS was 87.5 %, and 3-year DFS for secondary tumors was 44.7% (figure 33), so we found no significant difference in DFS in both groups (p value 0.310).

There were no statistical significant difference in OS and DFS between primary and secondary tumors.

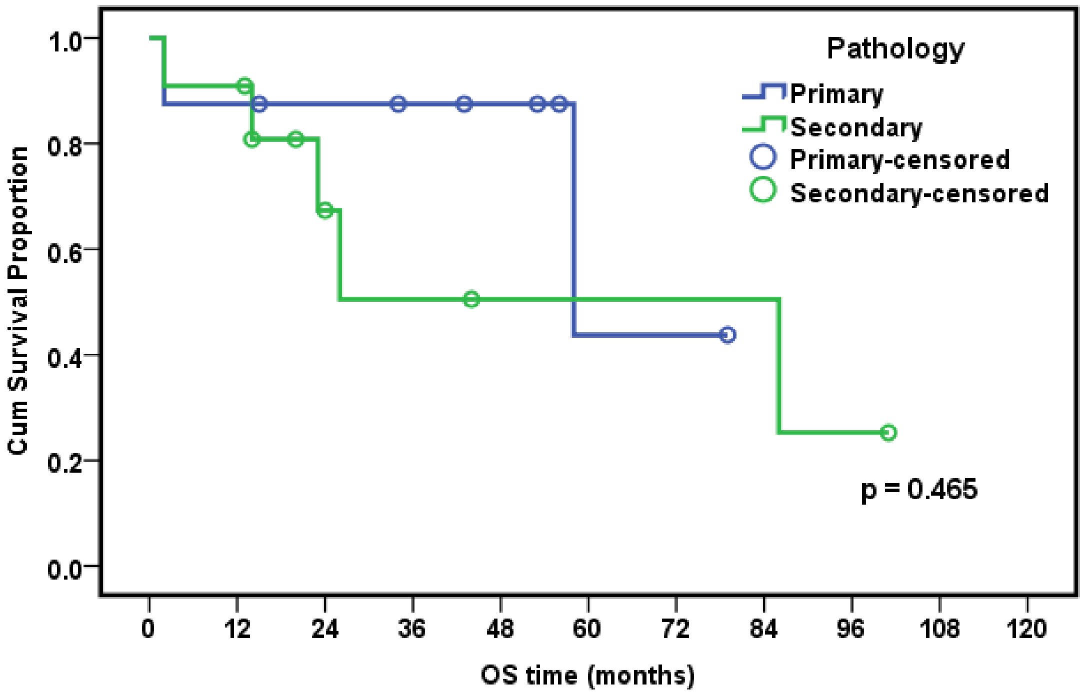

Figure 32. Overall Survival (OS) and its relation to pathological nature (primary versus secondary origin) as a prognostic factor.

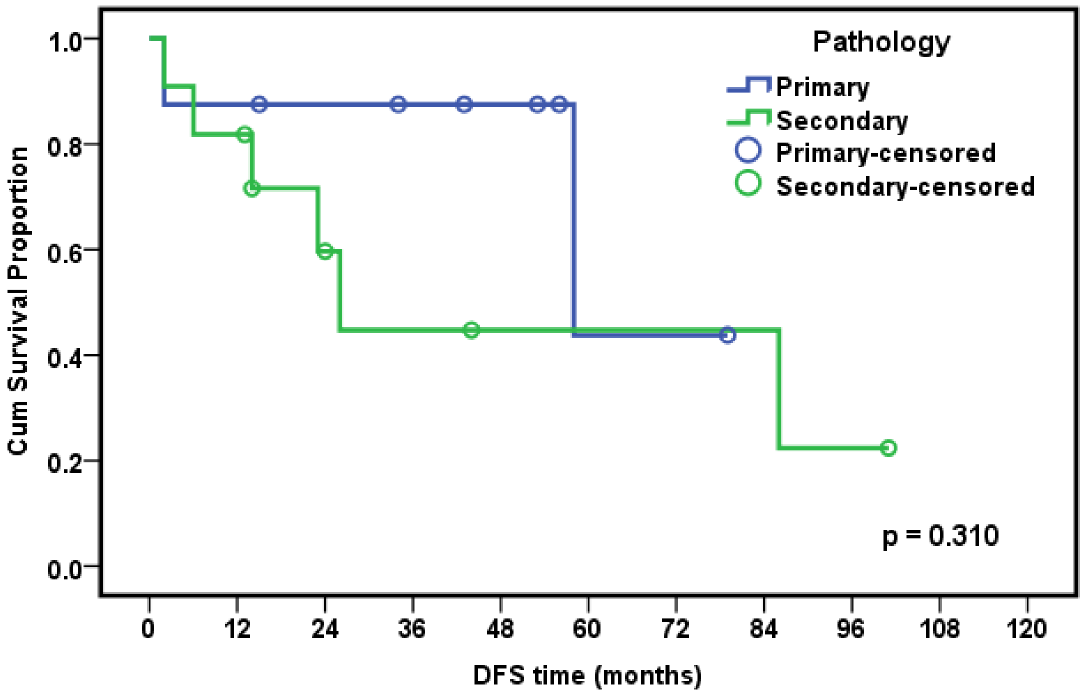

Figure 33. Disease Free Survival (DFS) and its relation to pathological nature (primary versus secondary origin) as a prognostic factor.

Three year OS in patients with breast origin secondary tumors was 31.3%, in comparison to non-breast secondaries three year OS was 80.0% (figure 34), then we found no significant difference in OS in both groups (p value 0.305).

Three year DFS in patients with breast origin secondary tumors was 25.0%, in comparison to non-breast secondaries 3-year DFS was 80.0% (figure 35), then we did not find significant difference in DFS in both groups (p value 0.193).

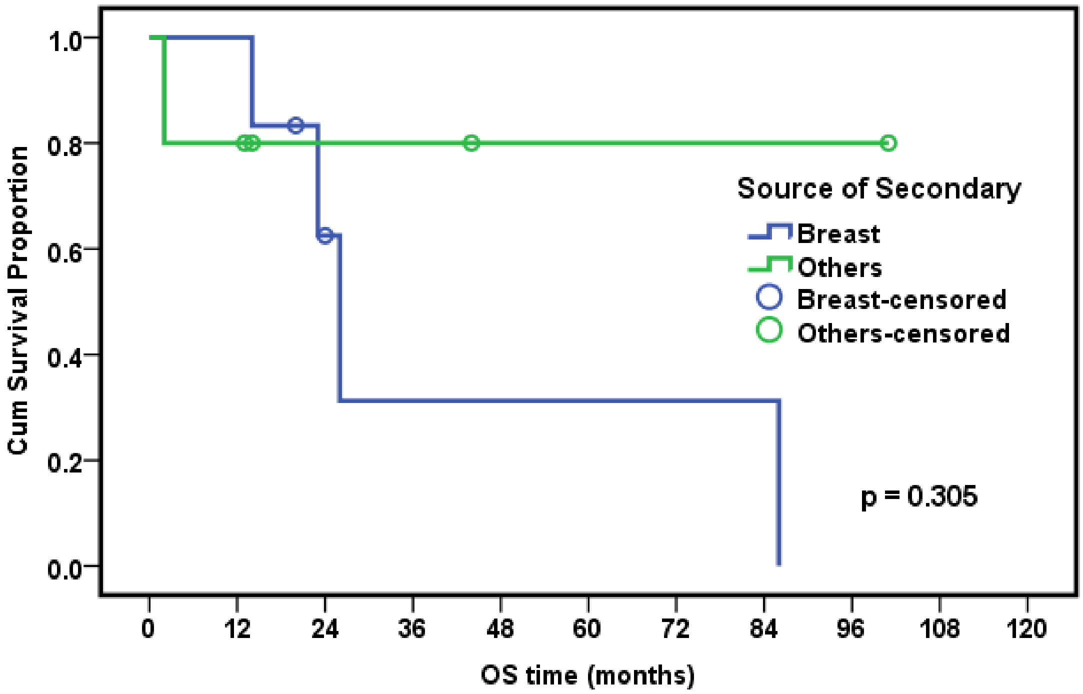

Figure 34. Overall Survival (OS) and its relation to pathological nature (secondary origin as breast versus other primary sites) as a prognostic factor.

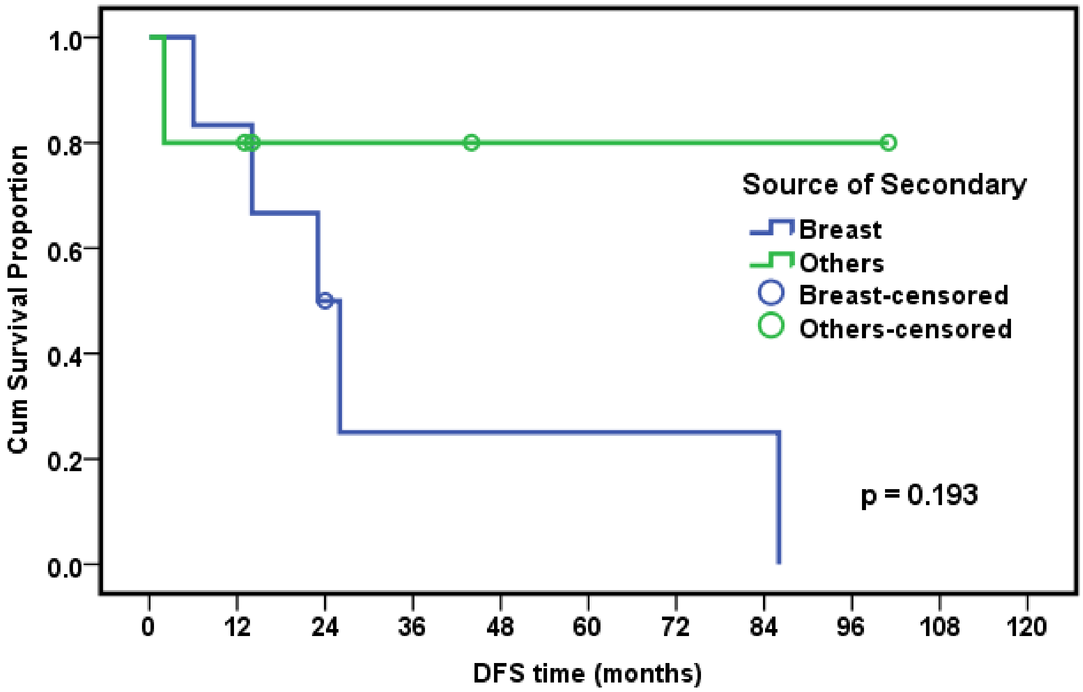

Figure 35. Disease Free Survival (DFS) and its relation to pathological nature (primary versus secondary origin) as a prognostic factor.

Patients diagnosed with negative margin at final pathology report were 16 out of 19 patients had one year OS for negative margin at final pathological report was 93.8%, two year OS for negative margin at final pathological report was 78.3%, and 3-year OS 78.3%, in comparison to those diagnosed with positive margin at final pathological report had one year OS for positive margin at final pathological report was 66.7%, two year OS for positive margin at final pathological report was 66.7%, and 3-year OS was 33.3% (figure 36).

Patients diagnosed with negative margin at final pathology report were 16 out of 19 patients one year DFS was 87.5%, two year DFS was 72.7%, and 3-year DFS was 72.7%, in comparison to the remaining 3 patient diagnosed with positive margin one year DFS for was 66.7%, two year DFS was 66.7%, and 3-year DFS was 33.3% (figure 37).

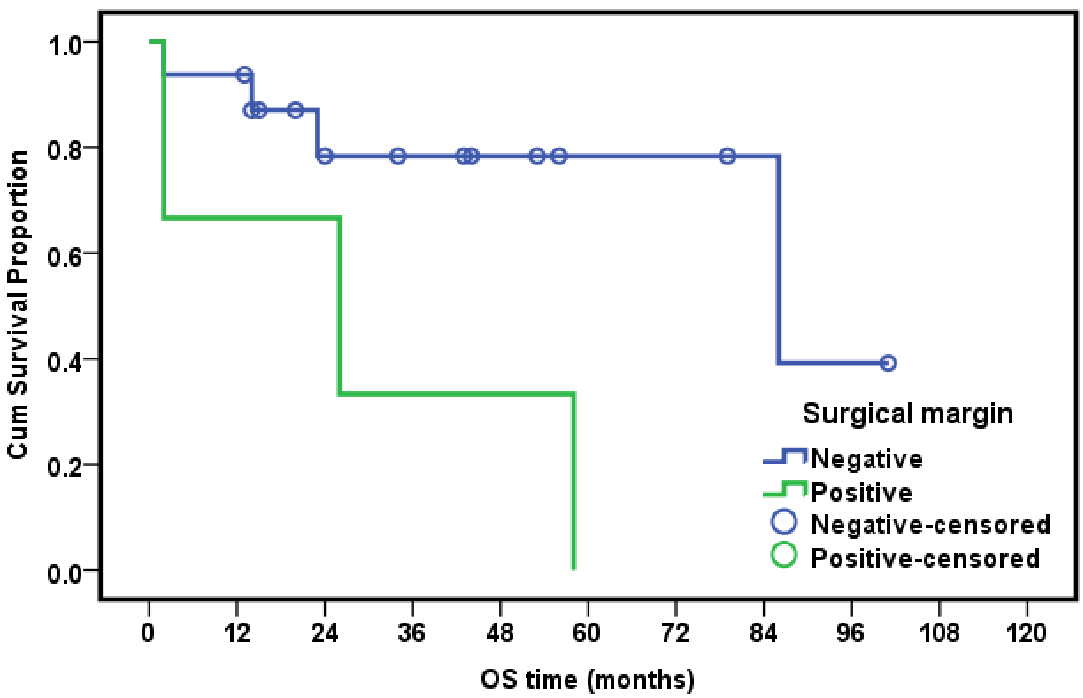

Figure 36. Overall Survival (OS) and its relation to pathological margin.

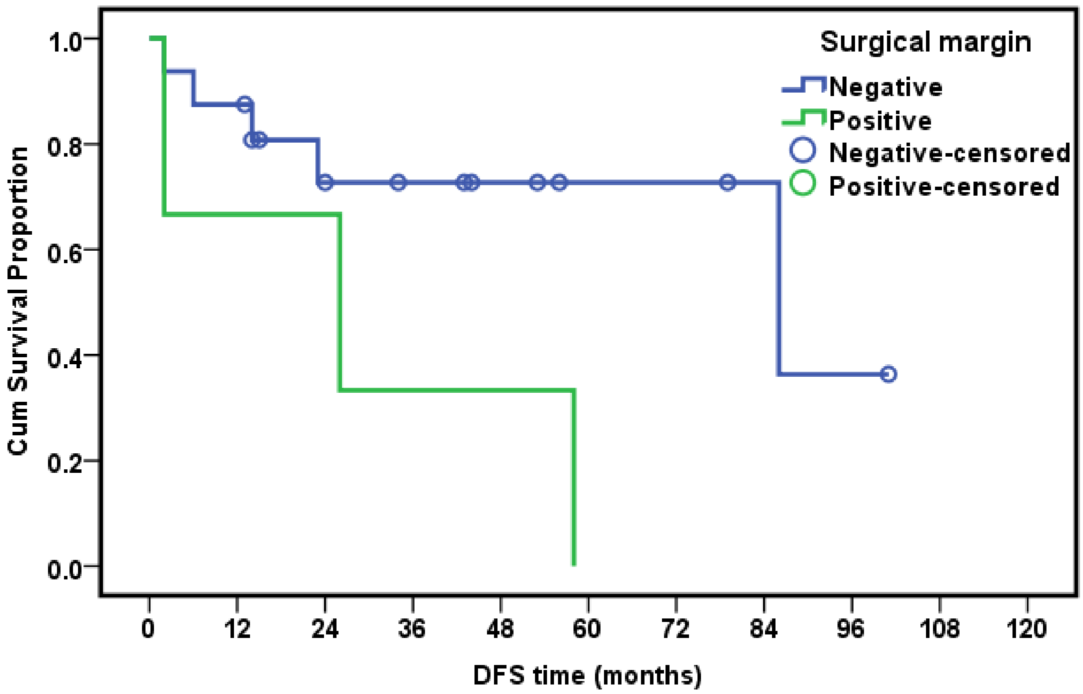

Figure 37. Disease Free Survival (DFS) and its relation to pathological margin.

We found that 3-year survival for low grade tumors was 100%, and 35% in high grade patients (figure 38). The difference between high and low grade was found to be statistically significant regarding OS (p value 0.015).

We found that 3-year DFS for low grade tumors was 100 %, and 30% in high grade patients (figure 39). The difference between high and low grade was found to be statistically significant regarding DFS (p value 0.007).

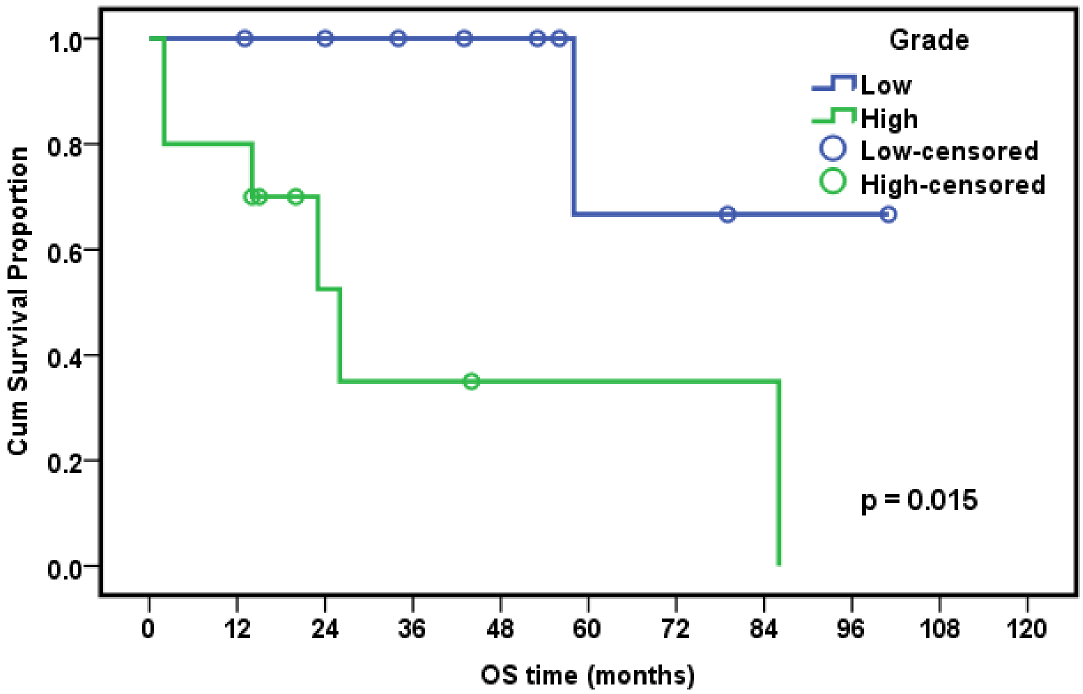

Figure 38. Overall Survival (OS) and its relation to pathological grade.

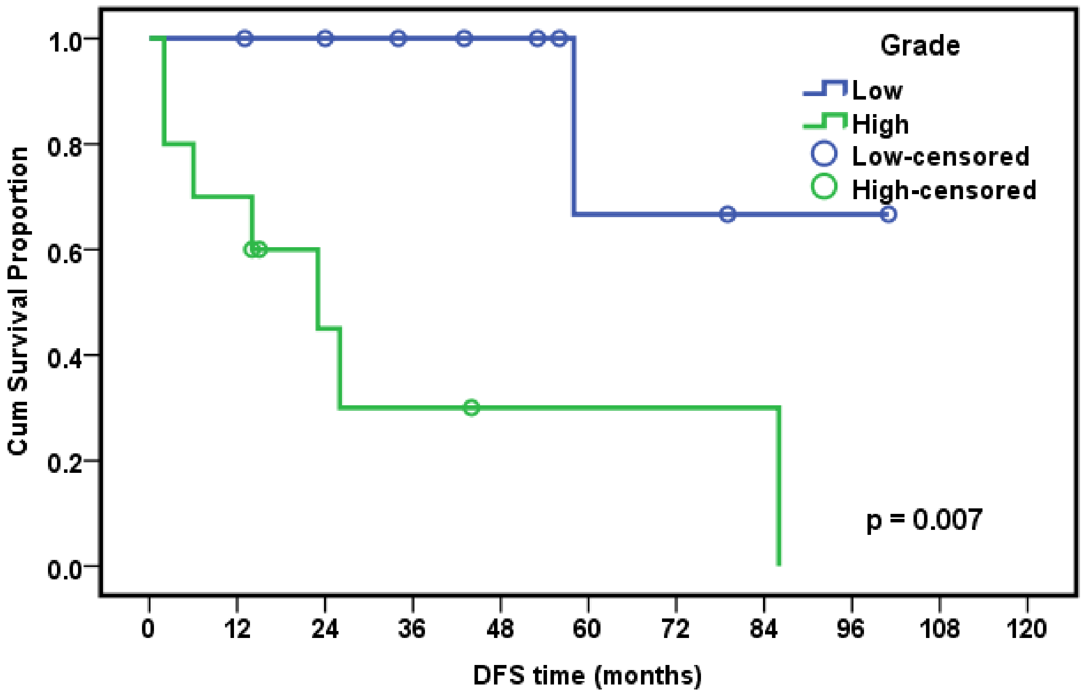

Figure 39. Disease Free Survival (DFS) and its relation to pathological grade.

By dividing patients according to maximum diameter of the sternal mass into 2 groups ,one of the equal or below than 6 cm ,the other above 6 cm we found 3-year DFS 66.6% and 66.7% respectively (figure 40), and so no significant difference was found in DFS in both groups (p value 0.776).

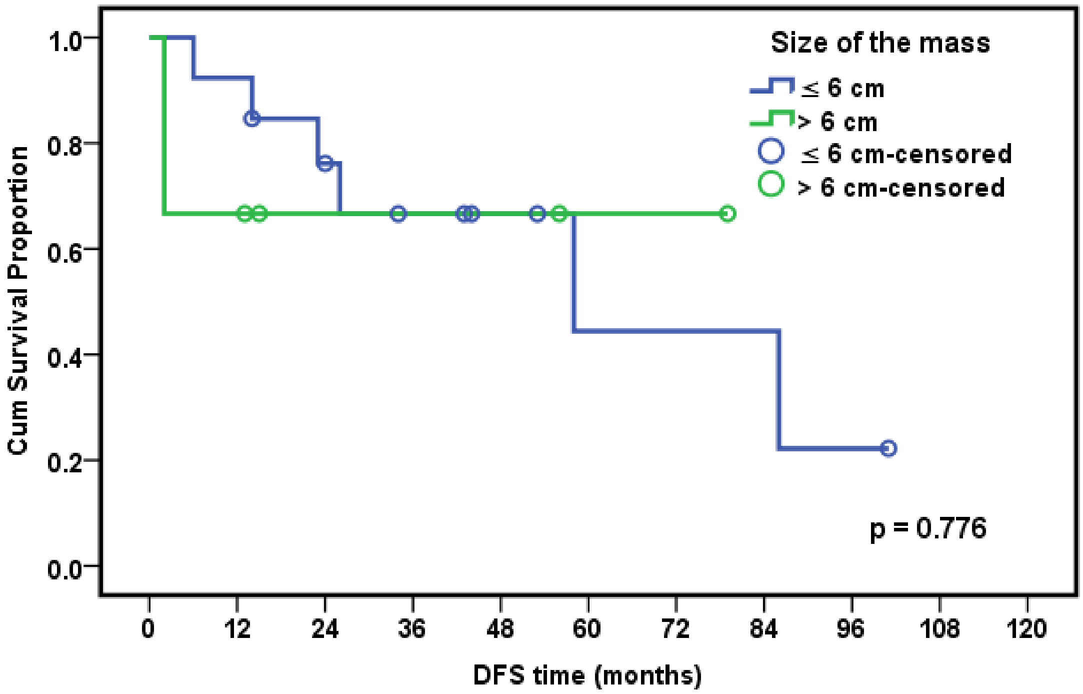

Figure 40. Disease Free Survival (DFS) and its relation to maximum mass diameter.

Three year OS for manubrium masses was 100%, 68.6% for lesions of upper part of the body of sternum, 37.5% for lesions occupying manubrium and upper part of sternal body and 100 % for lower sternal body lesions, 3-year OS was 0 % in lesions occupying the whole sternum (figure 41).

Three year DFS for manubrium masses was 80%, 68.6% for lesions of upper part of the body of sternum, 37.5% for lesions occupying manubrium and upper part of sternal body, 100% for lower sternal body lesions and 0% in lesions occupying the whole sternum (figure 42).

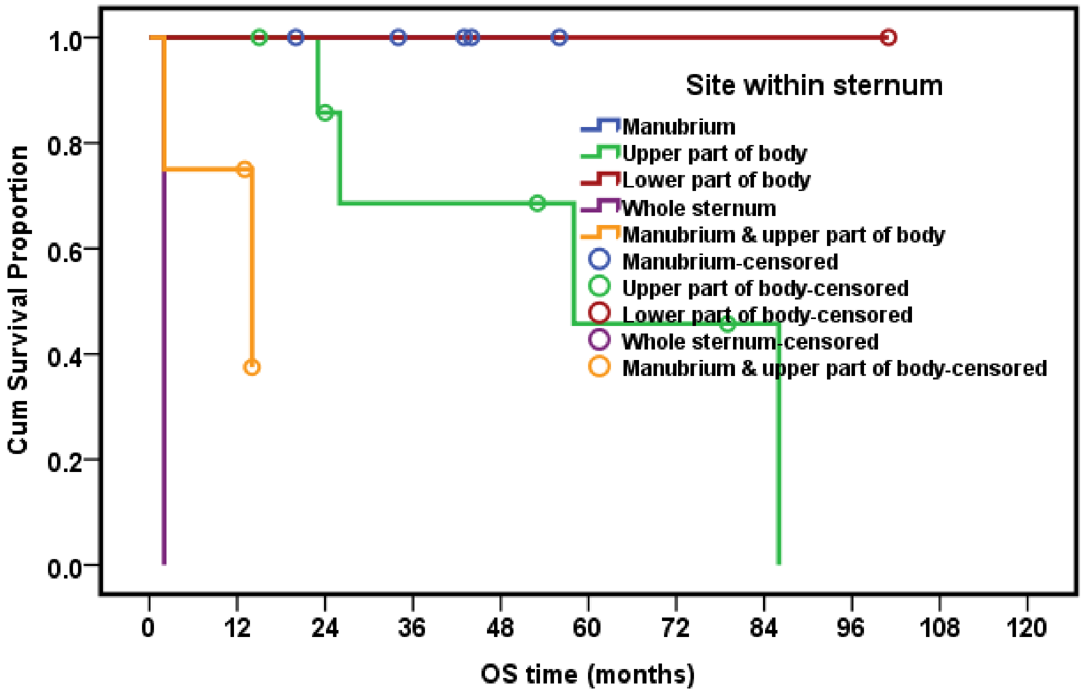

Figure 41. Overall Survival (OS) and its relation to mass location within the sternum.

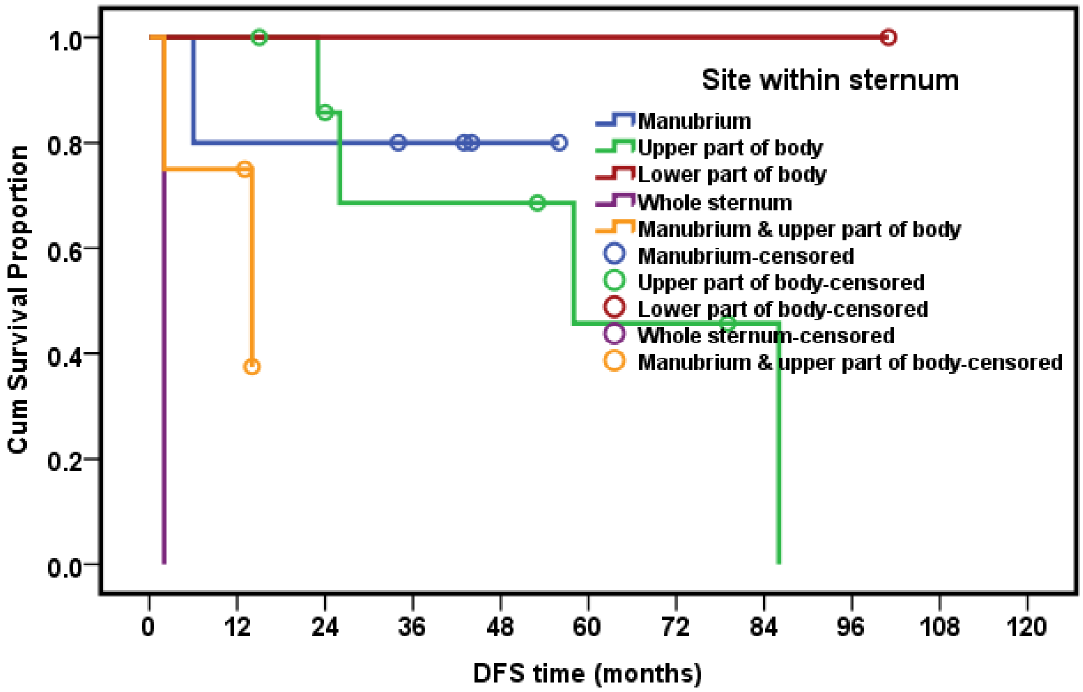

Figure 42. Disease Free Survival (DFS) and its relation to mass location within the sternum.

By dividing patients for whom sternectomy was done into 2 groups one of them there were resection to ribs, the other no rib resection was done. 3-year OS was 60% and 77.8% respectively (figure 43). This difference had no statistical significance in OS (p value 0.652).According to number of ribs resected during the sternal resection procedure, patients divided into 2 groups, the first group below than 5 ribs resected, the second group had 5 ribs or more resected the first group 3-year OS was 66.7%, in comparison to 50% in the second group.

Three year DFS was 52.5% and 77.8% respectively (figure 44). This difference had no statistical significance in DFS (p value 0.389). By categorizing patients for whom sternectomy was done into 2 groups one of them there were resection to 5 ribs or more, the other group less than 5 ribs resected. 3-year DFS was 50% and 55.6% respectively it was statistical insignificant in relation to DFS (p value 0.434).

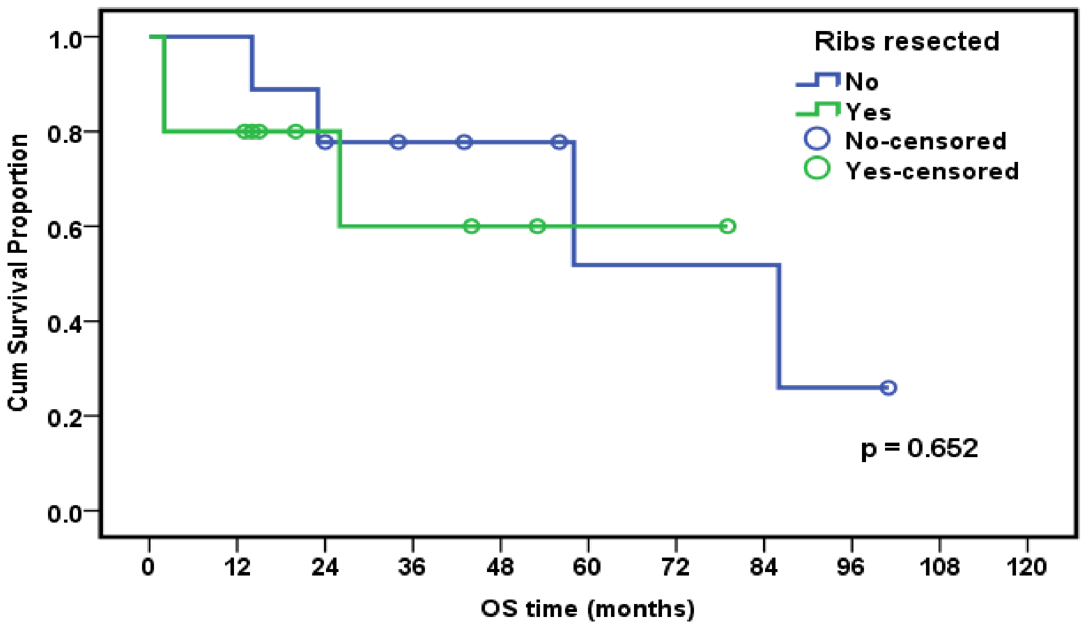

Figure 43. Overall Survival (OS) and its relation to resection of ribs.

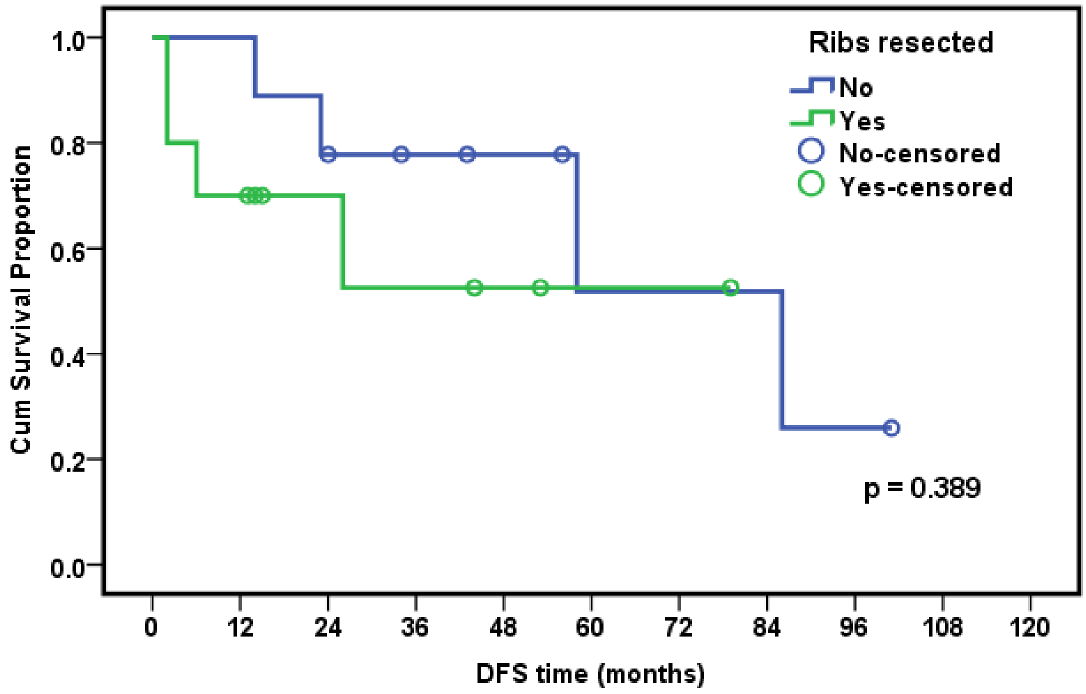

Figure 44. Disease Free Survival (DFS) and its relation to resection of ribs.

By categorizing patients for whom sternectomy was done into 2 groups one of them there were resection to nearby organs other than ribs as lung, pericardium, major vessels and clavicle were done, the other group no nearby organs resected. 3-year OS was 60% and 77.8% respectively (figure 45). No significant difference was found in OS in both groups (p value 0.652).

Three year DFS was 77.8% and 52.5% respectively (figure 46). No significant difference was found in DFS in both groups (p value 0.389).

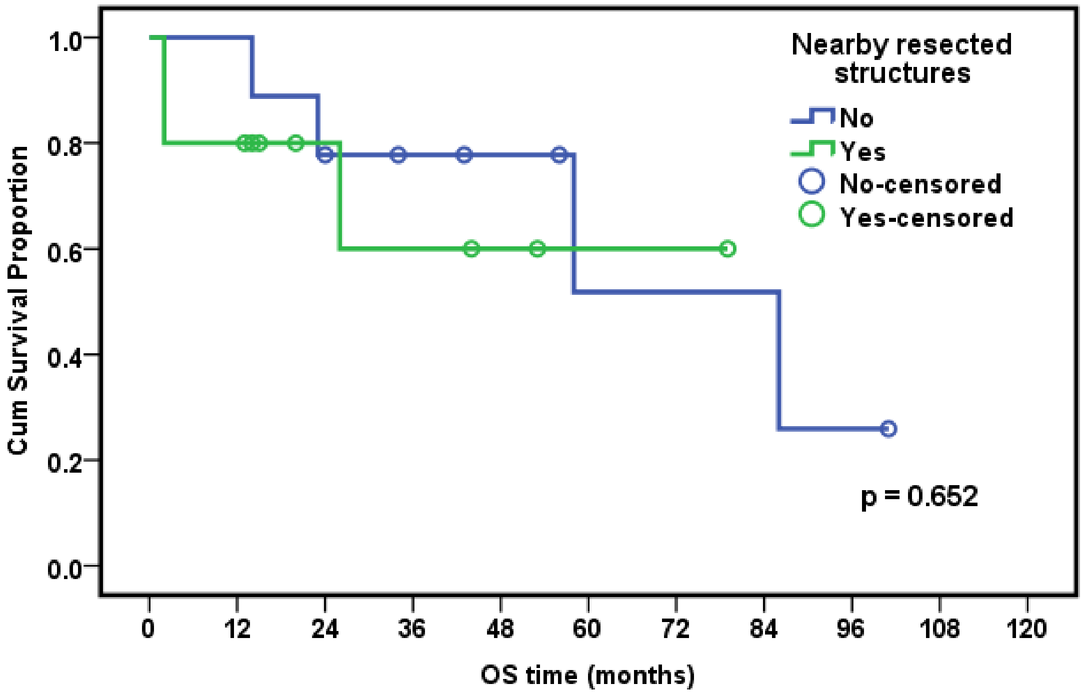

Figure 45. Overall Survival (OS) and its relation to resection of nearby structures.

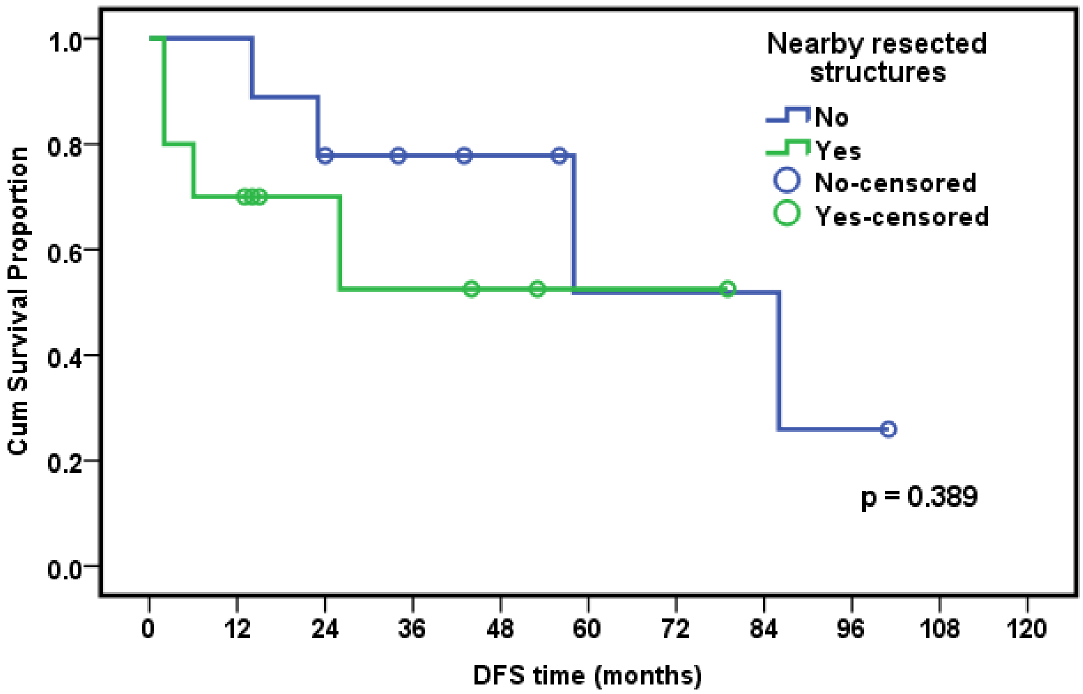

Figure 46. Disease Free Survival (DFS) and its relation to resection of nearby structures.

By categorizing patients into 2 groups one of them the defect size more than 100 cm² the other was below 100 cm². 3-year OS was 30% and 90% respectively (figure 47).The relation between defect size and OS showed a statistical significance (p value 0.012).

Three year DFS was 30% and 81.8% respectively (figure 48). The relation between defect size and DFS was a statistically near significant (p value 0.056).

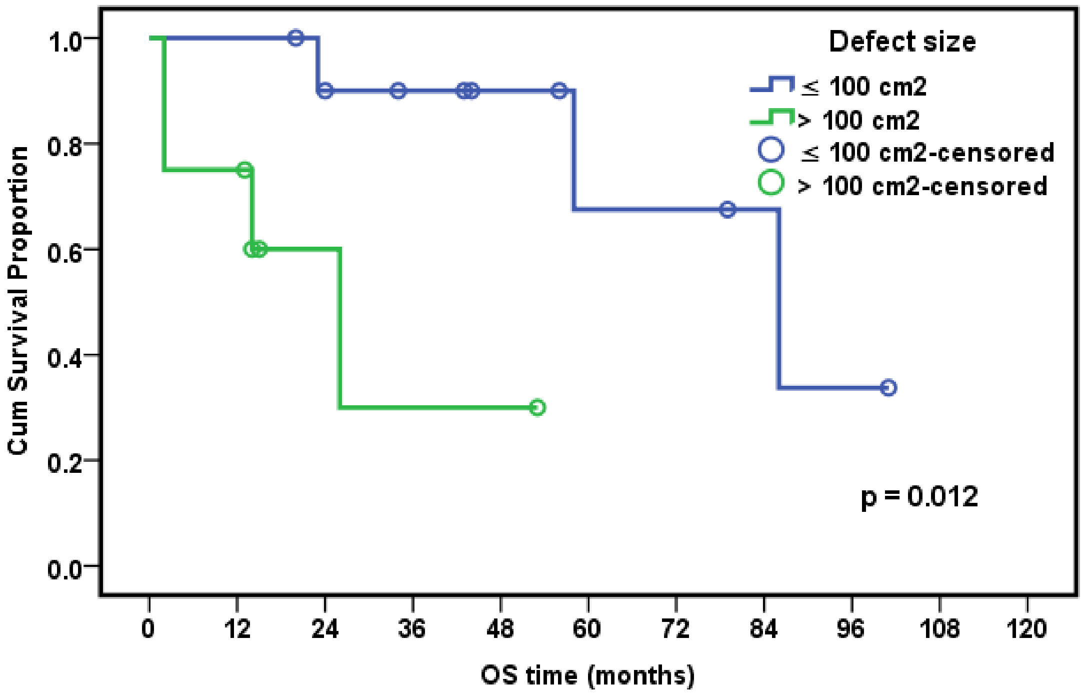

Figure 47. Overall Survival (OS) and its relation to defect size after resection.

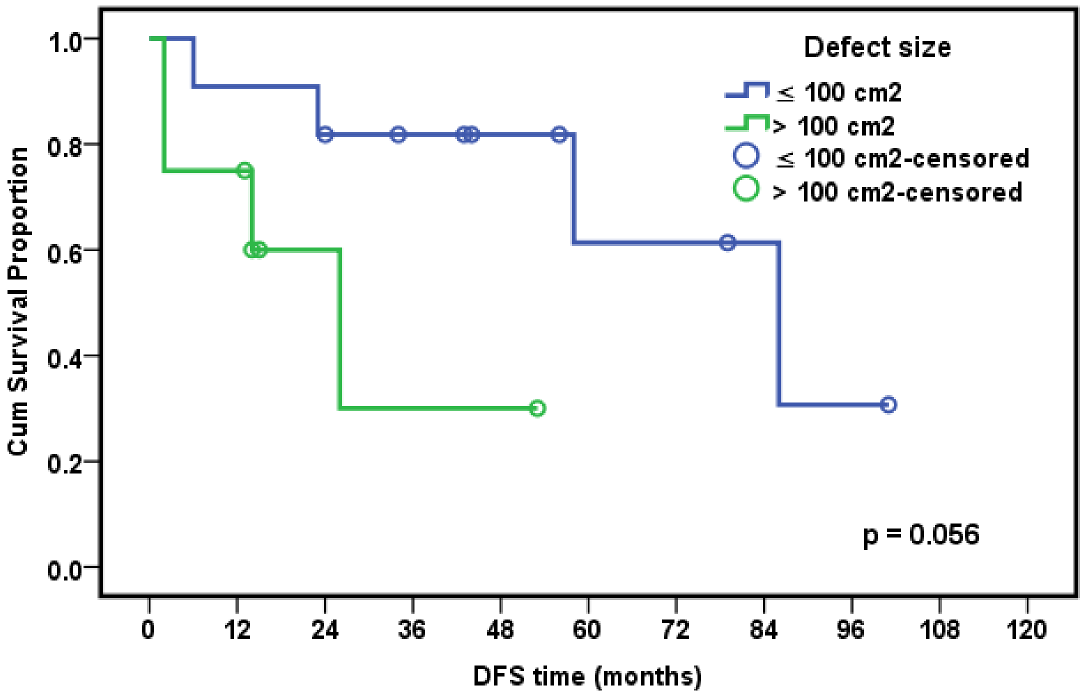

Figure 48. Disease Free Survival (DFS) and its relation to defect size after resection.

By dividing patients into 2 groups one of them received preoperative therapy and the other did not, 3-year OS was 55.6% and 80% respectively (figure 49). No significant difference was found in OS in both groups (p value 0.584).

Three year DFS was 48.6% and 80.0% respectively (figure 50). No significant difference was found in DFS in both groups (p value 0.0.359).

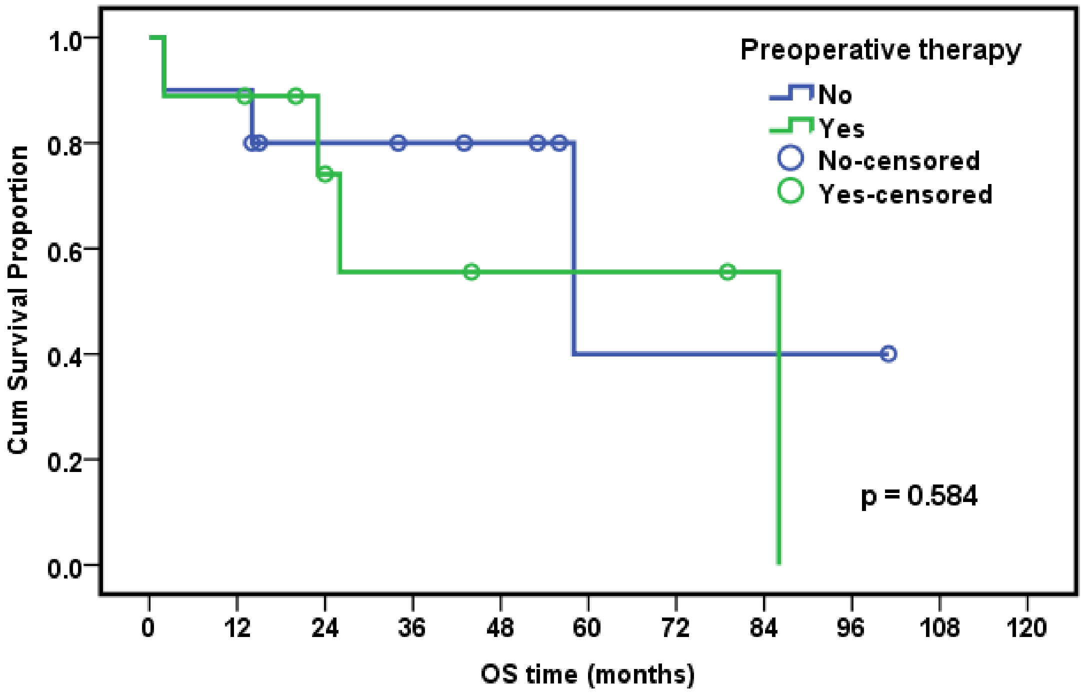

Figure 49. Overall Survival (OS) and its relation to preoperative therapy as a prognostic factor.

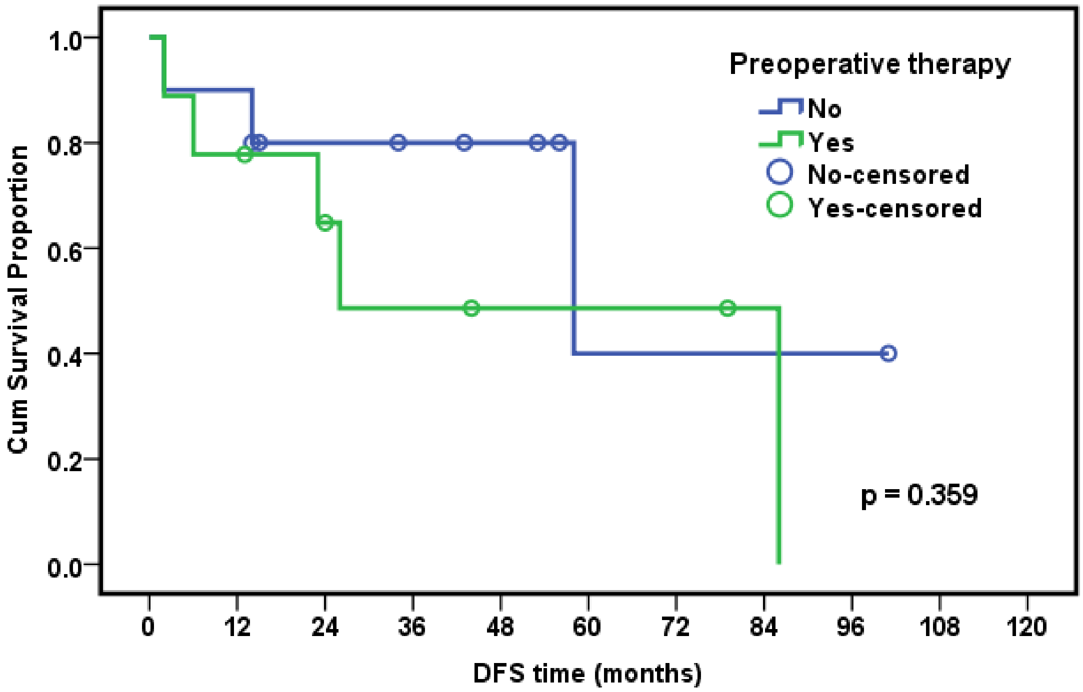

Figure 50. Disease Free Survival (DFS) and its relation to preoperative therapy as a prognostic factor.

Three year OS in patients who did not received adjuvant therapy postoperatively was 63.6%, in comparison to 100% three year OS in both who received either CTH (osteosarcoma patient) or radioactive iodine (metastatic follicular thyroid carcinoma patient) (figure 51).

Three year DFS in patients who did not receive adjuvant therapy post operatively was 58.7%, in comparison to 100% three year DFS for who received either CTH (osteosarcoma patient) or radioactive iodine (metastatic follicular thyroid carcinoma patient) (figure 52).

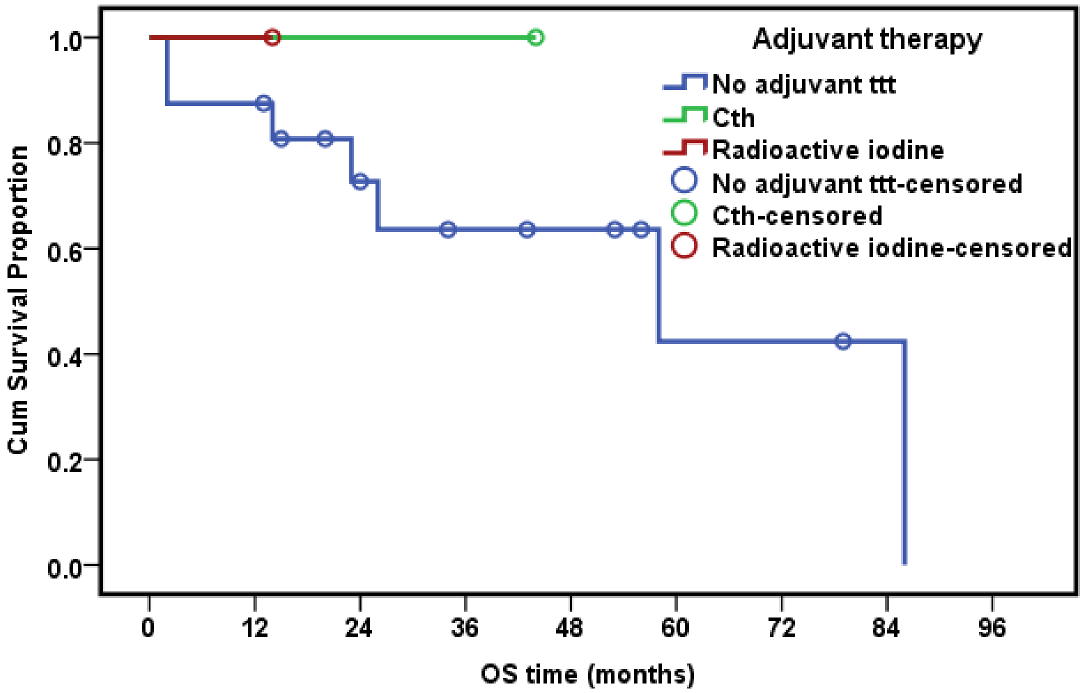

Figure 51. Overall Survival (OS) and its relation to adjuvant therapy as a prognostic factor.

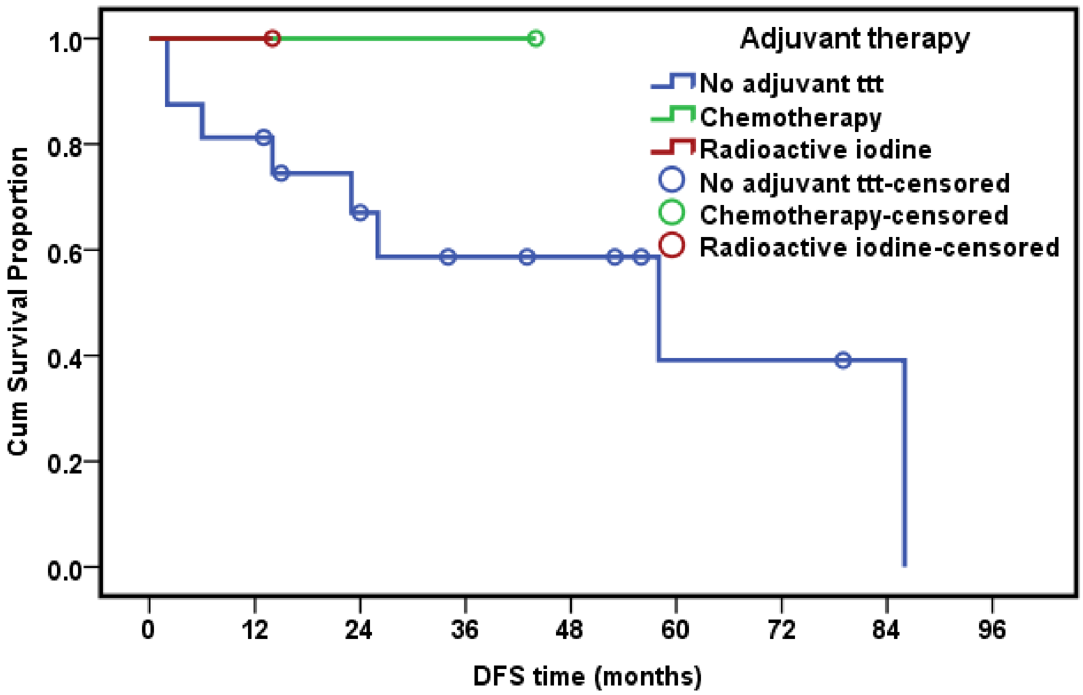

Figure 52. Disease Free Survival (DFS) and its relation to adjuvant therapy as a prognostic factor.

By dividing patients according to incidence of Complications other than respiratory complications, like local sepsis, DVT and hoarseness postoperative into 2 group, the first group did not have, and the second had, 3-year OS 76.2% and 50% respectively. The relation between incidence of Complications other than respiratory complications and OS showed a statistical significance (p value 0.033).

The difference between duration of ICU admission days and OS was found to be statistically significant (p value 0.040).

By dividing patients according to incidence of Complications other than respiratory complications, like local sepsis, DVT and hoarseness postoperative into 2 group, the first group did not have, and the second had, 3-year DFS 70.3% and 50.0 % respectively.

The relation between incidence of complications other than respiratory complications and DFS had no statistical significance (p value 0.077).

By categorizing patients for whom sternectomy was done into 2 groups one admitted in ICU for 1 or 2 days, the other group admitted for more than 2 days. 3-year DFS was 78.8 % and 40% respectively, the difference between duration of ICU admission days and DFS was found to be statistically significant (p value 0.040).

By categorizing patients for whom sternectomy was done into 2 groups one admitted in hospital 10 days or below, the other group admitted for more than 10 days. 3-year DFS was 81.8 % and 43.8% respectively. The relation between hospital admission days and DFS was found not to be statistically significant (p value 0.073).

Discussion

Sternal tumors are rare neoplasms. Resection with wide-free margins is an important prognostic factor, and massive CW resection and reconstruction are often necessary **(Foroulis CN et al., 2016).**

The evolution of surgical technique and the introduction in clinical practice of new prosthetic materials allowed larger resections, and safe and anatomical reconstruction **(Giuseppe M et al., 2014)**.

In our study, we found that the mean age of our patients was 40 years old and they ranged from 18 to 56 years old. 11 were males (52.4%) and 10 were females (47.6%).

This is similar to study done by Reza B et al, which included 40 patients, ratio of Males were equal to Females, with median age of 43.72 years **(Reza B et al., 2014).**

The size of maximum diameter of the sternal mass ranged from 4×3 to 22×5 cm. Median Maximum diameter of mass was 6 cm. Fifteen patient of the 21 (71.4%) of the study population were above or equal to 6 cm as maximum mass diameter.

Our figures comparable to those reported by Kitamura Y et al. who reported that Sternal masses ranged in size from 4 to 14 cm, with an average greatest dimension of 8.6 cm (**Kitamura Y et al., 1999)**.

Subtotal sternectomy was the most common procedure to be done, it was the procedure done in 13 patients (61.9%), partial sternectomy done in 6 patients (28.6%). Total sternectomy done only in 2 patients (9.5%). Median number of resected ribs was 4 ribs ranging from 1 to 8 ribs**.** Seven patients have organs with ribs have been resected (63.6%). Mostly, Clavicle was the commonest organ which had been resected along with ribs in 6 out of the 7 patients (85.7%).

This is similar to reports done by Alain RC et al. who reported in study done from 1986 to 2002 that 38 patients underwent radical resection of Primary Malignant Sternal Tumors. Eight total, seven subtotal, and 23 partial sternectomies were performed. Resection was extended to the anterior CW in 4 patients, lung in 4 patients, brachiocephalic vein in 3 patients, superior vena cava in 2 patients, and pericardium in 1 patient **(Alain RC et al., 2004)**

We found that, median defect size post excision was 88 cm^2 ranged from 25 to 432 cm^2.

These results comparable to a study performed by Omer S et al. who concluded that the area of reconstruction after sternectomy ranged from 35 to 264 cm^2. The technique of reconstruction included muscle flap alone in 13 patients; muscle flap and mesh, 9; muscle flap and rigid prosthesis , 7; or other, 1 patient **(Omer S et al., 1995).**

In our study, median Intra operative Blood transfusion was 2 units ranged from 1 to 5 units. Out of the 21 patients, eighteen of them needed intra operative blood transfusion.

Nine out of 16 (55.6%) patients underwent subtotal and partial sternectomy needed more than one unit packed RBCs, the remaining 7 needed only one unit .one of the two patients underwent total sternectomy needed one unit packed RBCs, the other patient needed more than one.

In a study performed by Mansour KA et al. concluded that Twenty-one patients underwent sternal resection and reconstruction. Management included partial sternectomy in 10 patients (group 1) and complete sternectomy in 11 (group 2). Blood transfusions averaged 2 units in group 1 versus 5.5 units in group 2 (**Mansour KA et al., 2002**).

After resection, reconstruction by rigid reconstruction done in 20 patients (95.2%). All of them of we use MMA and double polypropylene mesh in the form of “sandwich” prosthesis, in agreement with the a study performed by Foroulis CN et al. concluded that twenty patients were submitted to CW resection and reconstruction for malignant CW neoplasms between 2006 and 2014. The CW defect was reconstructed by using the “sandwich technique" (polypropylene mesh /methyl methacrylate/ polypropylene mesh) in nine cases of large anterior defects (**Foroulis CN et al., 2016)**.

In our study, soft tissue reconstruction was done in 14 patients (66.7%), 13 of them by pectoralis major myocutaneous flap (92.9%), only in one patient reconstruction done by omental flap (7.1%). in agreement with a study performed by Alain RC et al. concluded that from 1986 to 2002, 38 patients (25 females/13 males) underwent radical resection of Primary Malignant Sternal Tumors. Resection CW stability was obtained by Marlex or Vicryl mesh and polytetrafluoroethylene patch, with MMA reinforcement in 12 patients. Soft tissue coverage was done by the pectoralis major muscles with skin advancement in 25 patients, a myocutaneous flap in 11, a breast transposition in 1, and a skin flap in 1. Omentoplasty was performed in 3 patients **(Alain RC et al., 2004).**

Out of the 21 patients, thirteen of them had defect size after resection of the sternal mass equal or below than 100 cm did not raise need for post operative ventilation. The other group in which defect size more than 100 cm^2 was 8 patients, 5 of them (62.5% patients) did not need post operative ventilation, the other 3 patients (37.5%) needed postoperative ventilation.

Four out of the 21 patients (19%) complicated by pneumonia. Twenty out of the 21 patients had rigid reconstruction after sternectomy, 16 of the 20 patients (80%) did not complicated by pneumonia. The remaining 4 patients (20%) complicated by pneumonia, osteosarcoma patient was the only one who did not need rigid reconstruction, and he did not suffer from pneumonia.

In agreement with in a study performed by Michael JW et al. according to importance of defect size after resection and its effect on respiratory complications, as they concluded that IN From January 1, 1995, to July 1, 2003, 262 patients (median age, 60 years) underwent CW resection for tumor in 251 (96%), radiation necrosis in 7 (2.7%); and infection in 4 patients (1.3%), complicated by Respiratory failure occurred in 8 patients (3.1%). By multivariate analysis, the size of the CW defect was the most significant predictor of complications **(Michael JW et al., 2006).**

Their incidence of respiratory failure is lower than previously reported and may relate to our use of rigid repair for defects likely to cause a flail segment.

In our study, other complications occurred in 7 patients (33.3%). Four patients (57.1%) complicated by local sepsis. One patient complicated by SVC DVT, another one had hoarseness as a complication due to intentional resection of Rt. recurrent laryngeal nerve during sternectomy for osteosarcoma, the last patient complicated by mortality by day 10 postoperatively.

In a study performed by Alain RC et al. who concluded that, from 1986 to 2002, 38 patients (25 females/13 males) underwent radical resection of Primary Malignant Sternal Tumors complicated by one patient died from pneumonia, two patients needed a tracheostomy after total sternectomy. No flap-related complication was observed. Four local septic complications required removal of the composite prosthesis with reoperations. Local Recurrence occurred in 9 patients, 7 patients having a repeat resection. Metastases developed in eight **(Alain RC et al., 2004).**

We found that, all patients except one patient needed ICU admission, this patient was recurrent breast cancer. A Median ICU admission days were 2 days ranging from 1 to 10 days. Total hospital admission was below than or equal to 10 days in 12 patients (57.1%). Median hospital stay days was 10. Ranging from 6 to 25 day hospital admission was 25 days in 2 patients least hospital stay occurred in 3 patients was 6 days.

In agreement with results of the study performed by Dominique F et al. who concluded that the median ICU and hospital stay were 3.5 and 14 days **(Dominique F et al., 2012).**

In our study, chondrosarcoma was the most common type of sternal tumors in the 21 patients by 8 patients (38.1%).The 2nd most common type was recurrent breast cancer by 5 patients (23.8%). Sternal masses resected in this study were malignant in 19 patients (90.5%). Eleven of the 19 malignant cases (57.9%) were secondary tumors six of the 11 secondary tumors patients diagnosed as recurrent breast cancer invading or metastatic to sternum. All of clavicle, cervix, thyroid, mediastinum and bladder have one patient as a source of a tumor metastatic to sternum. Three of the 19 malignant cases was found to be positive margin. Ten out of 19 malignant masses was high grade.

In a study performed by Incarbone M et al. who concluded that the series included 20 primary malignant tumors, 4 desmoids tumors, 2 malignant tumors infiltrating the sternum from adjacent organs, 19 local recurrences or metastases of breast tumors, and 7 metastases of other tumors (**Incarbone M et al., 1997)**. The discrepancy in ratio between our study and this western study may be explained by limited number of our study cases.

Median Follow up period was 31 months, ranging from 2 to 124 months. Until now 14 patients out of 21 patient (66.7%) still alive during follow up visits.

We found that one year OS was 89.5 %. OS was 76.9 %. Two year, and three year OS was 69.2%.

Three year OS was 88.9% regarding male patients and 49.2% regarding female patients. The relation between gender and OS showed a statistical significance (p value 0.051).

Three year OS in our study better than results of a study performed by Incarbone M et al**.** who concluded that the overall 3-year survival was 58% and the 5-year survival 46%. In 24 patients with primary tumor the 5-year survival after radical resection was 63%, and in 23 patients with secondary invasion (direct extension or metastasis) the 5-year survival was 38% (median 35 months), recurrent breast cancer the 5-year survival was 48% in patients with direct extension to the CW. which is worse than our study 3-year OS, as our 3-year OS were primary tumors group 3-year OS was 87.5%,and secondary tumors group 3-year OS was 50.5%, but our patients must continue follow up to confirm this (**Incarbone M et al., 1997)**.

The better prognosis in our study may be explained by addition of recent adjuvant treatment especially in recurrent breast cancer patients.

Our results is comparable to results of a study performed by Omer S et al**.** who they concluded that Five-year actuarial survival after primary tumor resection was 73% and 33% after resection of recurrent breast cancer (median, 21 months) **(Omer S et al., 1995)**, which when compared to our results, we find our 3-year OS 87.5% and 31.3% for primary sternal malignant tumors and recurrent breast cancer invading the CW respectively,

In our study, recurrence occur after resection in 2 patients (9.5%).one of them was recurrent breast cancer suffered from local Recurrence which was treated with re surgery ,the other one diagnosed as chondrosarcoma had local and systemic recurrence.

We found that one year DFS was 84.2 %, two year DFS was 72%, and three year DFS for the 19 patient diagnosed with malignant disease to be 64.8%.

By dividing patients according to maximum diameter of the sternal mass into 2 groups, one of the equal or below than 6 cm, the other above 6 cm we found 3-year DFS 66.6% and 66.7% respectively, and so no significant difference was found in DFS in both groups (p value 0.776).

We found that 3-year DFS for low grade tumors was 100%, and 30% in high grade patients. The difference between high and low grade was found to be statistically significant regarding DFS (p value 0.007).

Patients diagnosed with negative margin at final pathology report was 16 out of 19 patients one year DFS was 87.5%, two year DFS was 72.7%, and 3-year DFS 72.7%, in comparison to the remaining 3 patient diagnosed with positive margin one year DFS for was 66.7%, two year DFS was 66.7%, and 3-year DFS 33.3%.

Three year DFS in patients who did not receive adjuvant therapy post operatively was 58.7%, in comparison to 100% three year DFS in who received either chemotherapy (CTH) (osteosarcoma patient) or radio active iodine (metastatic follicular thyroid carcinoma patient).

Comparable results were found in a study performed by Giuseppe M et al. who concluded that 5-and 10-year OS and DFS were 67.1 and 57.8%, and 70 and 52%, respectively. A favorable outcome (univariate analysis) was seen for diameter $\leq$ 6 cm ($P = 0.005$), G1 tumors ($P < 0.0001$), negative surgical margins ($P < 0.0001$), no adjuvant treatment ($P < 0.001$) **(Giuseppe M et al., 2014).**

Our study has some limitations: The number of patient was low due to the rarity of the disease and Data collected from records was relatively insufficient.

Summary

Sternal tumors are rare tumors, they are either primary tumors (malignant tumors, benign tumors), secondary tumors (carcinoma, sarcoma), adjacent neoplasms with local invasion and non-neoplastic diseases (cysts and inflammations).

Sternal tumors should be considered malignant till proved otherwise. Wide resection with tumor free margins is required in order to provide the best chance for cure in both benign and malignant lesions**.**

In this study, we report our recent experience with sternal tumors, and include a summary of the current literature to provide a reference for the management of this disease. We collected and analyzed retrospective data on the clinical presentation, radiologic imaging, pathology and operative details of patients with sternal tumors who underwent surgery at the National Cancer Institute between January 2005 and January 2015.

In all, 11of 21 patients were males, and the mean age of all patients was 40 years. The upper part of sternal body was the most common site affected by tumors, in 13 patients.

All patients were followed-up for a median Follow up period for 31 months. Ranging from 2 to 124 months. Nineteen patients out of 21 diagnosed as a malignant lesion, so we have statistically studied them by overall survival in relation to different prognostic factors.

We found that one year overall survival was 89.5 %, two and three year overall survival was, were 76.9 % and 69.2% respectively.

Patients diagnosed whom had negative margin at final pathology report was 16 out of 19 patients had one year overall survival for negative

margin at final pathological report was 93.8%, two year overall survival for negative margin at final pathological report was 78.3%, and three year overall survival 78.3%, in comparison to those whom had positive margin had one year overall survival for positive margin at final pathological report was 66.7%, two year overall survival for positive margin at final pathological report was 66.7%, and three year overall survival 33.3%.

Recurrence occur after resection in 2 patients (9.5%).one of them was recurrent breast cancer suffered from local Recurrence which was treated with re surgery, the other one diagnosed as chondrosarcoma had local and systemic recurrence. We found that one year disease free survival was 84.2 %, two year disease free survival was 72.0%, and three year disease free survival was 64.8%.

Twenty out of the 21 patients had rigid reconstruction after sternectomy to prevent flail chest.

Conclusion

Our conclusion is that sternal tumors are rare tumors, and should be considered malignant till proved otherwise. Wide resection with tumor free margins is required in order to provide the best chance for cure in both benign and malignant lesions. Surgical resection of malignant sternal tumors, followed by anterior chest wall reconstruction, is associated with favorable long-term overall survival and oncological outcomes.

Recommendations

We recommend to document patients' management data in the records regarding detailed history and proper examination, diagnostic work up, treatment delivered including surgery and CRT protocol, careful assessment with caring for follow up data and death certificates.

Finally, we recommend further multi institutional studies with a larger number of patients and longer follow up duration.

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الملخص العربى

ان اورام عظمه القص هي أورام نادرة، فهي إما أورام أولية (أورام خبيثة ,أورام حميده),أو أورام ثانوية (سرطانات انسجه, اورام لحميه) او أورام الاعضاء المتاخمة ذات طابع الغزو المحلي اوالأمراض غير الورمية (التكيسات والالتهابات).

تعتبر الأورام القصية خبيثة حتى يثبت العكس. يجب الاستئصال بحدود امان خالية من الورم من أجل توفير أفضل فرصة للشفاء في كل من الامراض الحميدة والخبيثة.

في هذه الدراسة، نسرد تجربتنا الأخيرة مع الأورام القصية، وتتضمن ملخصا للمواد العلميه المنشوره الحاليه لتوفير مرجع لعلاج هذا المرض. لقد جمعنا وحللنا البيانات بأثر رجعي على الاعراض السريرية، والتصوير الإشعاعي، والتفاصيل الباثولوجيه والجراحيه للذين يعانون من الأورام القصية الذين خضعوا لعمليات جراحية في المعهد القومي للسرطان فى الفتره من يناير ٢٠٠٥ وحتى يناير ٢٠١٥.

بشكل عام ، الزكور كانوا ١١ من ٢١ مريضا ، وكان متوسط العمر لجميع المرضى ٤٠ عاما. وكان الجزء العلوي لعظمه القص هو الموقع الأكثر شيوعا لحدوث الاورام وذلك في ١٣ مريضا .

شهرا. 124تراوحت بين الى تمت متابعة جميع المرضى فترة متوسط مدتها ٣١ شهرا . تسعة عشر من أصل ٢١ مريضا تم تشخيصهم على أنهم يعانون من مرض خبيث، لذلك قمنا بدراسة إحصائية لفتره بقائهم على قيد الحياة وارتباطها بالعوامل المنذره المختلفة.

وجدنا أن نسبه المرضى للبقاء سنة واحدة على قيد الحياة كان ٨٩,٥٪ , و سنتين و ثلاث سنوات على قيد الحياة، كانت ٧٦,٩٪ و ٦٩,٢٪ على الترتيب .

المرضى الذين تم تشخيصهم بتقرير تشريحى مرضي نهائي سالب الحدود كانوا ١٦ من أصل ١٩ مريضا كانت نسبه المرضى الذين بقوا على قيد الحياة لمده سنة واحدة ٩٣,٨٪ ، ولمدة و ثلاث سنوات كانت ٧٨,٣ ٪ ، بالمقارنة مع أولئك الذين كان لهم حد ٪ 78.3سنتين كانت إيجابي نسبه فتره بقاء سنة واحدة كان ٦٦,٧٪ ، و لمدة سنتين كانت ٦٦,٧٪ ، و ثلاث سنوات كانت ٣٣,٣٪ .

حدث ارتجاع بعد استئصال الورم لاثنين من المرضى (٩,٥٪). واحده منهم كانت تعانى من سرطان ثدي مرتجع ما بعد الجراحه ، والاخرى تم تشخيصها على أنها سرطان لحمى غضروفي

و كان ارتجاع محلية وعام . وجدنا أن نسبه المرضى الذين تعافوا من المرض لمده سنة واحدة كانت ٨٤,٢٪ ، ولمدة سنتين كانت ٧٢,٠٪ ، ولمده ثلاث سنوات كانت ٦٤,٨٪ .

عشرون من ٢١ مريضا تم إعادة البناء الصلب بعد استئصال عظمه القص لمنع الصدر السائب.

استنتاجنا هو أن الأورام القصية هي أورام نادرة، وينبغي النظر اليها على انها خبيثة حتى يثبت العكس. يجب استئصال الورم بحدود امان خالية من الورم من أجل توفير أفضل فرصة للعلاج في كل من الامراض الحميدة والخبيثة. الاسئتصال الجراحى للأورام القصية الخبيثة و إعادة بناء الجدار الأمامي للصدر ، وارتباطهما بالبقاء على قيد الحياة على المدى الطويل مده اطول وبنتائج ورميه افضل .

العلاج الجراحى لأورام عظمة القص
بالمعهد القومي للأورام
دراسه إكلينيكيه باثولوجيه لأورام عظمه القص
رساله للحصول على درجة الماجستير فى جراحة الأورام

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جامعة القاهرة

المعهد القومي للأورام

٢٠١٧