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ITMIG 2015

6th International Thymic Malignancy Interest Group Annual Meeting

Abstract Book

SHANGHAI, CHINA

OCTOBER 23–25, 2015

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ITMIG 2015

6th International Thymic Malignancy Interest Group Annual Meeting

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ORAL 1 - ABSTRACT SESSION 1: MOLECULAR BIOLOGY AND CHEMOTHERAPY

ORAL1.01: PHASE II TRIAL OF AMRUBICIN IN PATIENTS WITH PREVIOUSLY TREATED ADVANCED THYMIC MALIGNANCIES

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Background: Limited treatment options exist for patients with thymic malignancies (TM), and chemotherapy efficacy is often restricted by cumulative toxicity such as neuropathy (taxanes) and cardiomyopathy (anthracyclines). Single agent amrubicin, a third generation anthracycline and topoisomerase II inhibitor with minimal cardiac toxicity, was investigated in TM pts in this trial. **Methods:** This was an open-label single drug trial at 2 institutions in the United States (Stanford University and Indiana University). Eligible pts had TM (thymoma (T) or thymic carcinoma (TC)) with progression or relapse after at least 1 prior chemotherapy regimen, and adequate organ function including left ventricular ejection fraction (LVEF) of >50%. The initial treatment plan consisted of amrubicin at 40 mg/m^2 IV days 1-3 repeated in 3-week cycles. **Results:** From July 2011 to April 2014, a total of 33 patients (14T/19TC) were enrolled. There were 14 women and 19 men; age range of 30-81 years; 9 Asian, 1 African-American, 1 Hispanic and 22 non-Hispanic White pts. A high rate of febrile neutropenia (FN) led to an amended starting dose of 35 mg/m^2 days 1-3 repeated in 3-week cycles. In total, 7 pts experienced FN with 1 related death. Other grade 3/4 related events included: thrombocytopenia (n=2), neutropenia without fever (n=3), hyponatremia (n=2), hypokalemia (n=2), anemia (n=7), lethargy/fatigue (n=7), perirectal abscess (n=2), palmar-plantar erythrodysesthesia (n=3), syncope (n=2), venous embolism (n=2), and 1 pt each with sepsis, oral abscess, mucositis, chest pain, and epigastric pain. Other toxicities were generally mild and well tolerated. No significant changes in LVEF were noted on serial echocardiograms. There were 6 partial responses (4T/2TC), 21 with stable disease, and 4 with progressive disease (PD) or death at or before first assessment for a response rate (RR) of 18% and a disease control rate (DCR) of 88% (29%/11% RR in T vs TC and 100%/78% DCR in T vs TC). All but 5 patients received at least 4 cycles, and 15 tolerated >10 cycles, with 38 cycles as the highest number to date. Three patients remain on therapy. Conclusions: Amrubicin, at 35 mg/m^2 IV days 1-3 on a 3-week cycle, shows promise as a single agent in pre-treated patients with thymoma and thymic carcinoma with an 18% RR (29% thymoma/11% thymic carcinoma) and no unexpected toxicity. Disease control rates of 100% in the thymoma patients and 78% in the thymic carcinoma patients were observed. Response rate and disease control rate were higher in the thymoma patients compared to the thymic carcinoma patients. Further exploration of amrubicin as a single drug or in combination is warranted in thymic malignancies.

Keywords: amrubicin, thymoma, thymic carcinoma, chemotherapy

ORAL1.02: SUNITINIB IN PATIENTS WITH ADVANCED THYMIC EPITHELIAL TUMORS (TET)

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Background: No standard treatments are available for advanced TET after failure of first-line platinum-based chemotherapy. Sunitinib is a potent oral tyrosine kinase inhibitor of VEGFR, KIT and PDGFR. In a single arm phase 2 study of sunitinib after at least one previous line of chemotherapy, a 26% of partial response rate (PR) was reported in thymic carcinoma (TC) and 6% in thymoma (T), with a median progression free survival (mPFS) of 7.2 months and 8.5 months, respectively. We investigated if off-labelled prescription of sunitinib in this population induced the same efficacy signal. **Methods:** We investigated the RYTHMIC database of the French thymic malignancies network. We reviewed advanced T and TC patients (p) who were treated with sunitinib in order to evaluate patient's outcome. **Results:** From October 2011 to January 2015, 28 patients from 7 institutions were identified (20 TC and 8 T). Nine out of 28 p (32%) were females and median age was 49.7 y. Fifteen patients (54%) received sunitinib in ≥ 4th line of treatment. Two patients received sunitinib in 1st line treatment (1 T and 1 TC). The 37.5 mg was the initial dose of sunitinib in 16p. In the whole population, the DCR (partial / complete response and stable disease) was 61%. DCR was 55% in TC (11 out of 20p) and 75% in T (6 out of 8p). The ORR rate was 21% (4 out of 20p with TC (20%) had a PR; and 2 out of 8p with T (25%) had PR). Of note, PR to sunitinib was independent of treatment line (1p at 1st lines, 1p at 3rd line, 2 p at 4th line and 2p at ≥ 5th line) and sunitinib initial dose (for 3p initial dose of sunitinib was 37.5 mg and for 3p was 50 mg). 3 TC p were c-KIT positive, without a clear relationship with response rate (1 PR, 2 PD). The mPFS in whole population was 103 days. For TC the mPFS was 87 days and 139 days for T. The median overall survival (OS) in the whole population was 175 days, with prolonged OS in T vs. TC (403 days vs. 166 days). Sunitinib adverse events were manageable and tolerable. 8p stopped sunitinib due to toxicity of whom 2 had achieved PR. **Conclusion:** Sunitinib is an active treatment in TET irrespective of histological subtype and treatment line, even in a heavy pre-treated population, supporting antiangiogenic therapies as an alternative treatment option for these patients.

Keywords: Efficacy, Thymic, Tumors, Sunitinib

ORAL1.03: FREQUENT PD-L1 EXPRESSION IN THYMIC SQUAMOUS CELL CARCINOMA OF CHINESE PATIENTS

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Background: A recent publication reported diffuse high intensity PD-L1 staining in thymic epithelial tumor (TET).The PD-L1 scores and histology were significantly correlated, with higher intensity staining in WHO classification B2/B3/C TET. Among B2/B3/C TET. Thymic squamous cell carcinoma (TSQCC) has morphological features of squamous cell carcinoma as seen in other organs. Unlike thymomas, it generally lacks resemblance to the normal thymic cytearchitecture. Here we examine PD-L1 expression in a thymic squamous cell carcinoma of Chinese patients. **Methods:** Fifteen (15) TSQCC specimens obtained from the Shanghai Chest Hospital

tissue archive were stained with Merck Serono anti-PD-L1 antibody MKP1A07310 on Ventana's (instead of Dako) core reagent and instrumentation platform. Scoring of PD-L1 expression on a semi-quantitative scale was performed by a trained surgical pathologist, who is blinded to clinical data and sample identity. The percentage of tumor cells expressing membrane PD-L1 immuno-reactivity at the intensities weak (1+), moderate (2+), and strong (3+) will be recorded. **Results:** Strong PD-L1 expression was observed in 5 specimens (30%). A focal (instead of diffuse) staining pattern on tumor cell membrane (instead of both membrane and cytosol) was observed. The medial age with positive expression of TSQCC was 61 years old, and 60% was male. Tumour stage at strong PD-l1positive was IIA, III, IV Respectively in 20%, and stage IIB in 40%. Conclusions: PD-L1expression was present in thymic squamous cell carcinoma. Strong expression was observed in 30%. The correlation of the clinic-pathological parameters and PD-L1 expression in TSQCC should be research.

Keywords: PD-L1, thymic tumor, histology

ORAL 1 - ABSTRACT SESSION 1: MOLECULAR BIOLOGY AND CHEMOTHERAPY

ORAL1.04: MICRORNA NETWORKS: NOVEL KEY REGULATORS IN THYMIC EPITHELIAL TUMORS

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Thymic epithelial tumors (TET) are the most frequent human primary mediastinal tumors. For invasive and/or relapsing cases no effective treatment regimens have been definied, as relevant pathways are still not known. A biological characterization of the relevant molecules related to the pathogenesis and progression of neoplastic tissue in TET is strongly needed. MicroRNAs (miRNAs) constitute a large group of negative gene regulators playing an important role in carcinogenesis in several tumor systems. Mature microRNAs (miRNAs) are single-stranded RNA molecules of 20- to 23-nucleotide (nt) length controlling gene expression in many cellular processes We recently identified a group of mature miRNAs differentially expressed in tumor versus normal thymic tissues by microarray analysis of 54 formalin-fixed paraffin embedded (FFPE) thymic tumors and 12 normal counterparts (1). In particular, we found 56 microRNAs that were up-regulated and 31 down-regulated in thymic tumors. We found that a subgroup of these miRs was also differentially expressed among the different tumor histotypes. Finally, by bioinformatics analysis we identified molecular pathways whose members are putatively targeted by TET-associated miRNAs and that could impact on TET biology. We performed an Affimetrix-based study on a series of fresh frozen thymoma and normal thymi samples from our series. A deeper characterization of the identified pathways involved in TET carcinogenesis by the identification of the key molecular interactions is in progress. Our preliminary data support a key regulator role of mature MicroRNA in TET.

F. Ganci, C. Vico, E. Korita et al., MicroRNAs Expression Profiling of Thymic Epithelial Tumors –- Lung Cancer 85 (2) (2014) 197–20404

Keywords: MicroRNA, Thymoma, Thymic carcinoma, Thymic Epithelial Tumors

ORAL 2 - ABSTRACT SESSION 2: TREATMENT AND NOVEL APPROACHES

ORAL 2 - ABSTRACT SESSION 2: TREATMENT AND NOVEL APPROACHES

ORAL2.01: PROTON BEAM RADIATION THERAPY FOR ADJUVANT AND DEFINITIVE TREATMENT OF THYMOMA AND THYMIC CARCINOMA

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Introduction: Radiation therapy is a critical component of treatment for thymic tumors. However, radiation-induced toxicity may reduce benefit, particularly in the adjuvant setting. Proton beam therapy (PBT), due to its characteristic Bragg peak, is ideally suited to treat the anterior mediastinum while sparing organs at risk. To date, PBT to treat thymic tumors has only been reported in three single-patient case studies. In this study, we evaluated patterns of failure and toxicity in patients treated for thymoma and thymic carcinoma using PBT and hypothesized that PBT can achieve excellent local control with limited high grade toxicity. **Materials and Methods:** All patients with thymoma or thymic carcinoma treated with PBT between 2011-2015 were analyzed. Either double scattered proton therapy (DS-PT) or pencil beam scanning (PBS) were used. Toxicity was assessed using CTCAE v 4.2. Local control, distant control, and overall survival were analyzed by the Kaplan-Meier method from the time of PBT completion. **Results:** Twenty-seven patients were included (Table). Patients were a median age of 56 years, predominantly female (56%), and had thymoma (85%) or thymic carcinoma (15%). They were treated with definitive (22%) or salvage (15%) PBT or adjuvant (63%) PBT following resection with predominantly close (23%) or positive (50%) margins. Forty-one percent also received chemotherapy. Patients were treated to a median of 61.2Gy (range 50.4-70.2Gy) using DS-PT (85%) or PBS (15%). Median mean lung dose, volume of lung receiving ≥20Gy (V20), and V5 were 98cGy (1-2050cGy), 18% (0-38%), and 26.2% (0-55%). Median mean heart and esophagus doses were 1065cGy (105-3356cGy) and 1072cGy (0-4655cGy). No patient experienced grade ≥3 acute or chronic toxicity. Acute grade ≥2 toxicities included fatigue (11%), esophagitis (7%), dermatitis (37%), and pneumonitis in one patient (4%) who received 2 prior thoracic radiotherapy courses. Late grade ≥2 toxicity was limited to a single patient with chronic dyspnea (grade 2). At a median follow-up of 1.8 years, 100% local control was achieved. Regional control rates at 1, 2, and 3-years were 96% (95% CI 76-99%) and distant control was 85% (95% CI 59-95%), 85% (95% CI 59-95%), and 74% (95% CI 41-90%). Two unresectable patients (B3, C histologies) died from disease progression, with overall survival at 1, 2, and 3 years of 96% (95% CI 73-99%), 89% (95% CI 61-97%), and 89% (95% CI 61-97%). **Conclusion:** PBT in the definitive, adjuvant, and salvage treatment of thymoma and thymic carcinoma has very low acute and chronic toxicity and excellent 3-year outcomes.

Longer follow-up and additional studies are required to determine whether PBT has improved clinical outcomes over photon therapy.
Table:

Characteristics		**Number of patients(%)**
Age at diagnosis	Median, years (range)	56 (29-78)
Sex	Male	12 (44)
	Female	15 (56)
Tumor Histology	A	2 (7)
	AB	6 (22)
	B1	7 (26)
	B2	1 (4)
	B3	5 (19)
	C	4 (15)
	Unknown	2 (7)
Tumor size	Median, cm (25th and 75th percentile)	5.05 (3.8, 7.17)
Masaoka stage	I	3 (11)
	II	16 (29)
	III	2 (7)
	IV	6 (22)
Radiation intent	Definitive	6 (22)
	Adjuvant	17 (63)
	Salvage	4 (15)
Margin status	Negative	4 (15)
	Close	5 (19)
	Positive	11 (41)
	No surgery	7 (26)
Radiation Dose (cGy)	5040-5940	9 (33)
	6120-6600	13 (48)
	≥7000	5 (19)
Chemotherapy	Neoadjuvant	6 (22)
	Concurrent	5 (19)
	Adjuvant	4 (15)
	None	12 (44)

Keywords: Thymoma, thymic carcinoma, Proton therapy, External beam radiation

ORAL 2 - ABSTRACT SESSION 2: TREATMENT AND NOVEL APPROACHES

ORAL2.02: THE ROLE OF POSTOPERATIVE RADIOTHERAPY FOR STAGE I/II/III THYMIC TUMOR--RESULTS OF CHART DATABASE

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Background: Postoperative radiotherapy for thymic tumor is still controversial. The object of the study is to evaluate the role of postoperative radiotherapy for stage I/II/III thymic tumor. **Methods:** The database of Chinese Alliance of Research for Thymomas (ChART) was retrieved for patients with stage I/II/III thymic tumor who underwent surgical therapy without neoajuvant therapy between 1994 and 2012. Univariate and multivariate survival analyses were performed. Cox proportional hazard model was used to determine the hazard ratio for death. **Result:** 1546 stage I/II/III patients were identified from ChART database. Among these patients, 649 (42.0%) underwent postoperative radiotherapy. Postoperative radiotherapy was associated with gender, histologic type (World Health Organization, WHO), surgical extent, complete resection, Masaoka stage and adjuvant chemotherapy. The 5-year and 10-year overall survival (OS) rates and disease-free survival (DFS) rate for patients underwent surgery followed by postoperative radiotherapy were 90% and 80%, 81% and 63%, comparing with 96% and 95%, 92% and 90% for patients underwent surgery alone ($p = 0.001$, $p < 0.001$) respectively. The 5-year and 10-year recurrence rate for patients underwent surgery followed by postoperative radiotherapy were 18% and 35%, comparing with 7% and 8% for patients underwent surgery alone ($p < 0.001$). In univariate analysis, age, histologic type (WHO), Masaoka stage, completeness of resection, and postoperative radiotherapy were associated with OS. Multivariable analysis showed that histologic type (WHO) ($p = 0.001$), Masaoka stage ($p = 0.029$) and completeness of resection ($p = 0.003$) were independently prognostic factors of OS. In univariate analysis, myasthenia gravis, age, gender,histologic type (WHO), Masaoka stage, postoperative radiotherapy, surgical approach, tumor size and completeness of resection were associated with DFS. Multivariable analysis showed that histologic type (WHO) ($p < 0.001$), Masaoka stage ($p = 0.005$) and completeness of resection ($p = 0.006$) were independently prognostic factors of DFS. Subgroup analysis showed that patients with incomplete resection underwent postoperative radiotherapy achieved better the 5-year and 10-year OS and DFS ($p = 0.010$, 0.017, respectively). Postoperative radiotherapy did not affect the OS of patients with Masaoka stage I/II/III who underwent complete resection ($p = 0.067$, 0.615 and 0.192, respectively). **Conclusion:** The current retrospective study indicated that postoperative radiotherapy after incomplete resection could improve OS and DFS for patients with stage I/II/III thymic tumor.

Keywords: thymic tumor, postoperative radiotherapy, survival

ORAL 2 - ABSTRACT SESSION 2: TREATMENT AND NOVEL APPROACHES

ORAL2.03: S-1 SALVAGE TREATMENT FOR CHEMOREFRACTORY STAGE IV THYMIC CARCINOMA: A REPORT OF 19 CASES

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Background: It remains challenging to deal with progression disease of thymic carcinoma after previous systemic chemotherapy. By now, there are a few case reports from Japanese authors about the effects of S-1 on such patients. In this study, we reported the clinical outcome of S-1 as a salvage chemotherapy in a larger number of patients. **Methods:** Patients, pathologically diagnosed as thymic carcinoma, were enrolled in this study when confirmed with extensive lesions. All patients had to receive at least one regimen of chemotherapy and showed disease progression before considering the choice of S-1. The following eligibility criteria should be met: PS score≤2; leukocyte count≥3.0x10^9/L; platelet count≥80 x10^9/L . The capsules were taken orally twice daily at a dose of 60-70mg/m2 per day for 2 weeks, followed by 1-week drug-free interval. Each cycle contains four-week drug application and two-week interval. The cycles would be repeated unless disease progressed or intolerable adverse effect was confirmed. **Results:** From January 2011 to April 2015, totally 19 patients (male: female=9:10) have been included in this study with a median age of 56(27-75). The majority of pathological subtype is squamous cell carcinoma (15 cases). There are also 2 undifferentiated carcinoma, 1 lymphoepithelioma-like carcinoma and 1 high grade neuroendocrine carcinoma. Eight patients had metastasis in lung, 4 in liver, 3 in lymph nodes and 2 in brain. Another 4 patients failed in pleural dissemination. Before S-1, all patients received first-line chemotherapy, 14 out of 19 patients received second-line chemotherapy, and 3 patients received third-line chemotherapy. The average cycles applied in all patients are 3.4, ranging from 1-12. The overall response status are partial response 3(16%), stable disease 13(68%) and progression disease 3(16%). The median progression free survival is 5 months (0-15). Among the 3 patients with progression disease, 2 have brain metastasis, and the other one is neuroendocrine carcinoma. The main toxicity over grade 2 are appetite loss in 9 (47.3%), platelet count dropping in 4 (21%) and hemoglobin leveling down in 2 (10%). Most of the side effects are moderate and do not lead to drug suspension. **Conclusion:** S-1 could be used as an effective salvage chemotherapy for extensive thymic carcinoma to relieve symptoms and to extend survival span with low toxicity. But it seems that patients with brain metastasis or those classified as neuroendocrine carcinoma could not benefit from this regimen.

Keywords: S-1, chemotherapy, thymic carcinoma

ORAL 2 - ABSTRACT SESSION 2: TREATMENT AND NOVEL APPROACHES

ORAL2.04: EXPRESSION AND SIGNIFICANCE OF C-KIT AND EMT MOLECULES IN THYMIC EPITHELIAL TUMORS

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Objective To investigate the expression and significance of c-kit and EMT molecules (E-cadherin, N-cadherin, Twist, Snail) in thymic epithelial tumors. **Method** By using the tissue microarray technology and immunohistochemistry MaxVision™-use kit to detect the expression of c-kit and EMT molecular markers (E-cadherin, N-cadherin, Snail, Twist) in 150 cases of paraffin sections of thymic epithelial tumor tissue, Analysis the correlation between c-kit and EMT molecules; explore the malignancy degree and clinicopathological parameters relationship between c-kit, EMT molecules and thymic epithelial tumors. **Results** The difference of c-kit positive expression in thymoma between the subtypes (A 9.09%, AB 2.86%, B1 5.26%, B2 5.00%, B3 8.70%) was no statistically significant (P>0.05); While the positive expression rate of thymic carcinoma 68.18% (15/22) was significantly higher than thymoma 5.47% (7/128), the difference between them was statistically significant (P<0.01). The difference of E-cad positive expression in thymoma between the subtypes (A 81.82%, AB 85.71%, B1 78.95%, B2 80.00%, B3 73.91%) was no statistically significant (P>0.05); The positive expression rate of thymoma 80.47% (103/128) was significantly higher than thymic carcinoma 22.73% (5/22), the difference between them was statistically significant (P<0.01). The difference of N-cad positive expression in thymoma between the subtypes (A 0%, AB 0%, B1 5.26%, B2 5.00%, B3 8.70%) was no statistically significant (P>0.05); The positive expression rate of thymic carcinoma 63.64% (14/22) was significantly higher than thymoma 3.91% (5/128), the difference between them was statistically significant (P<0.01). The difference of Twist positive expression in thymoma between the subtypes (A 18.18%, AB 14.29%, B1 21.05%, B2 20.00%, B3 21.74%) was no statistically significant (P>0.05); The positive expression rate of thymic carcinoma 72.73% (16/22) was significantly higher than thymoma 18.75% (24/128), the difference between them was statistically significant (P<0.01). The difference of Snail positive expression in thymoma between the subtypes (A 9.09%, AB 8.57%, B1 15.79%, B2 12.50%, B3 21.74%) was no statistically significant (P>0.05); The positive expression rate of thymic carcinoma 77.27% (17/22) was significantly higher than thymoma 13.28% (17/128), the difference between them was statistically significant (P<0.01). c-kit expression and E-cad expression was negatively correlated; c-kit expression and N-cad, Twist, Snail was positively correlation. E-cad expression and N-cad, Twist, Snail was negatively correlation. N-cad expression was positively correlated with Twist, Snail. Twist and Snail expression was positively correlated. **Conclusion** 1. The expression of c-kit, E-cadherin, N-cadherin, Twist and Snail in each tissue subtype of thymoma were no significantly differences; While their expression between thymic carcinoma and thymoma were statistically significant, suggesting that these five indicators may help to determine the malignant degree of thymic epithelial tumors. 2. The expression of c-kit and E-cad was negatively correlated while the expression of c-kit with N-cad, Twist and Snail was positively correlated, suggesting that overexpression of c-kit may promote the EMT process of thymic epithelial tumors. 3. The expression of Twist and Snail was positively correlated, suggesting that Twist and Snail may have a synergistic effect, both of them combined expression can better promote tumor metastasis.

Keywords: thymic epithelial tumors; c-kit; EMT; Snail; Twist

ORAL 3 - ABSTRACT SESSION 3: REGIONAL TRENDS

ORAL 3 - ABSTRACT SESSION 3: REGIONAL TRENDS

ORAL3.01: MALIGNANT THYMOMA INCIDENCE IN A CHINESE POPULATION

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Background Malignant thymoma is a rare malignancy of unknown etiology. Few population-based studies have described the patterns of the incidence. **Objective** Describe the incidence of malignant thymoma and its trend in Shanghai, a representative sample of Chinese urban population, to provide basic information on the future clinical and prevention research. **Methods** Overall incidence and age specific incidence of malignant thymoma by sex and area (central downtown and suburb) in Shanghai in 2007-2011 were calculated to describe the current pattern. Annual percent change (APC) of age-standardized rates of the population in central downtown from 1973 to 2011 was analyzed with Poisson regression. **Results** The

overall incidence of malignant thymoma in 2007-2011 was 6.3 per 100,000 person-years (Total 444 cases, 88 cases averagely per year) and the age-standardized rate was 3.6per 100,000 person-years in Shanghai. The histopathology confirmed cases account for 76.6% (340 cases) of all the cases. Among the histopathology confirmed cases, 71.4% were thymic epithelial. The age-specific incidence increased with age except the age groups above 75.There is no significant difference of overall age-standardized rates (ASR) between male and female. The ASR in central downtown is higher (39%) in suburb. In the central downtown area, the age-adjusted incidence rates in the male and the female were 1.2 and 0.6 per 100,000 person-years in 1973-1977, and increased to 4.7 and 3.8 per 100,000 person-years in 2007-2011. The annual percentage changes were 4.0% and 5.2% of male and female respectively during the past 39 years.

Malignant Thymoma Incidence in Shanghai during 2007-2011

Population	Sex	Cases	Overall rates /100 000	Age-standardized rates /100 000
Total	Male and female	444	6.3	3.6
	Male	239	6.8	3.9
	Female	205	5.9	3.3
Central downtown	Male and female	227	7.7	4.3
	Male	122	8.3	4.7
	Female	105	7.1	3.8
Suburb	Male and female	217	5.4	3.1
	Male	117	5.8	3.3
	Female	100	4.9	3.0

Conclusions Malignant thymoma is extremely rare in Shanghai as well as in most other area of the world; however its incidence is increasing constantly in the recent 4 decades. Diagnosis improvement may explain part of the variation of the incidence, while further exploration on causation and risk factors are warrant.

Keywords: malignant thymoma, Chinese, incidence, cancer registry

ORAL 3 - ABSTRACT SESSION 3: REGIONAL TRENDS

ORAL3.02: POSTOPERATIVE SURVIVAL FOR PATIENTS WITH THYMOMA COMPLICATING MYASTHENIA GRAVIS--CHART EXPERIENCE

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Objectives: To compare the postoperative survival between patients with thymoma only and those with both thymoma and MG. **Methods:** The CHART registry recruited patients with thymoma from 16 centers over the country on an intention to treat basis from 1994 to 2012. Two groups were formed according to whether the patient complicated MG. Demographic and clinical data were reviewed, Patients were followed and their survival status were analysed. **Results:** There were 1179 patients included in this study, including 206 with and 973 without MG. Complete thymectomy were done in 85.9% patients in MG group and 64.4% in non-MG group P<0.05.There were more percentage of patients with the histology of tumors of thymoma AB, B1,or B2 P<0.05 in MG group, and more percentage of patients with MG were in Masaoka's stage I and II. The 20 year overall survival rates were 74.6% and 72.1% respectively(P=0.051)(FIGURE 1). The survival rate was significantly higher in patients with MG when the histology was thymoma B3 or C **P=0.0083**, or when the Masaoka's staging was 3 or 4 **P=0.0089** (FIGURE 2).

FIGURE 1. Postoperative survival curves according to the presence of myasthenia gravis(MG) .

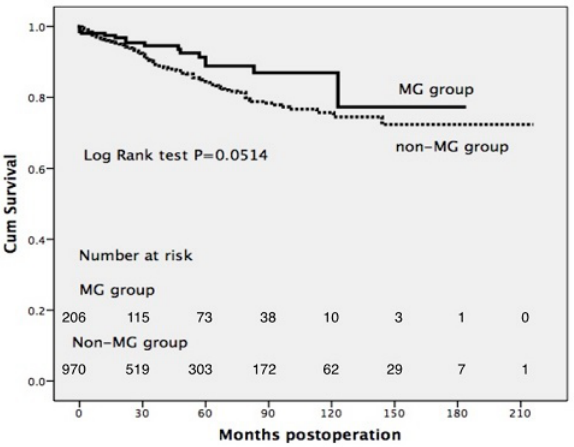
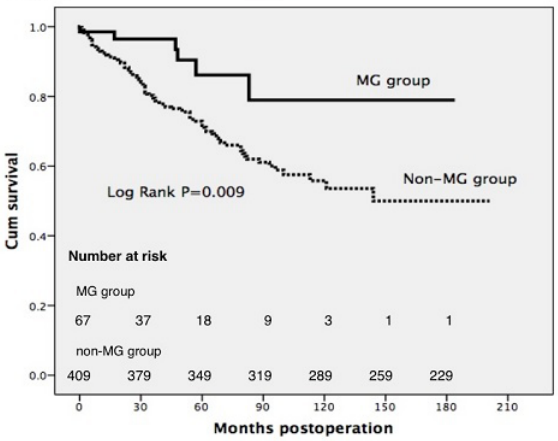


FIGURE 2. Postoperative survival curves in Masaoca 3/4a/4b patients for MG group and Non-MG group.



Among patients with advanced stage thymoma (stage 3, 4a, 4b), the constituent ratios of 3,4a,4b were similar between MG and Non-MG group. Histological, however, there were significantly more proportion of B1/B2 in the MG group while there were more B3/C in the non-MG group **(P=0.000).**Both groups were comparable in terms of resectability and postoperative recurrence, except that total thymectomy had been done in more proportion of patients in MG group **(P=0.021).** Multivariate analyses of Cox regression for all patients showed, Masaoka's stage and resectability were strong independent prognostic indicators. Whereas in late Masaoka's stage patients, MG and resectability were strong independent prognostic indicators. The OR for MG(yes) was 0.332 compared to non-MG**. (P=0.019) Conclusions** The survival of patients with thymoma was superior when MG was present, especially in late Masaoca's stage patients. Possible reasons included early diagnosis of the tumor, better pathologic types and more attention for complete thymectomy in this group.

Keywords: Thymoma, myasthenia gravis, survival

ORAL 3 - ABSTRACT SESSION 3: REGIONAL TRENDS

ORAL3.03: INCREASING NUMBER OF THYMECTOMIES PERFORMED IN THE UNITED STATES

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Background: Thymoma is a relatively rare disorder, but the true incidence in the United States is unknown because only cases described as "malignant" or "invasive" on final pathology reports are included in cancer registry data. An increasing number of thymomas may be identified incidentally on CT scans done for other purposes. As minimally invasive techniques have become more prevalent, thymectomy may also be offered for more patients. For these reasons, we hypothesized that the use of thymectomy has increased in the U.S. in recent years. **Methods:** Using the Nationwide Inpatient Sample (NIS) from 1998-2011, we identified 6457 patients who underwent thymectomy as a primary procedure. We also used the Surveillance, Epidemiology and End Results (SEER) database to identify the incidence of malignant thymoma from 1998-2011. Ordinary least squares regression was performed to assess trends in the incidence of thymectomy and malignant thymoma. **Results:** From 1998 to 2011, the incidence of thymectomy per 100,000 admissions increased from 4.4 to 6.6 with annual increase of 3.6% (p = 0.002, Figure 1). A total of 2,132 cases of malignant thymoma were reported in SEER from 1998-2011. There was not an increase in the incidence of malignant thymoma (p=0.14, Figure 2). From 2009-2011, 22% (n = 362) of thymectomies were performed thoracoscopically and 9.1% were performed robotically (n = 146). **Conclusion:** The number of thymectomies performed in the U.S. has increased in recent years. This does not appear to correspond to a definite increase in the incidence of malignant thymoma. It is unclear whether the true incidence of thymoma is increasing or whether thymectomy is simply becoming more common. This data demonstrates the need for more comprehensive reporting of thymomas and we advocate inclusion of all thymomas in cancer registry data.

Figure 1. Annual incidence of thymectomies performed in the United States 1998-2011 (per 100,000 admssions) in Nationwide Inpatient Sample.

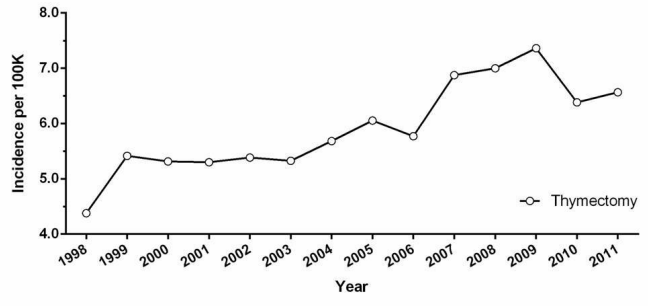
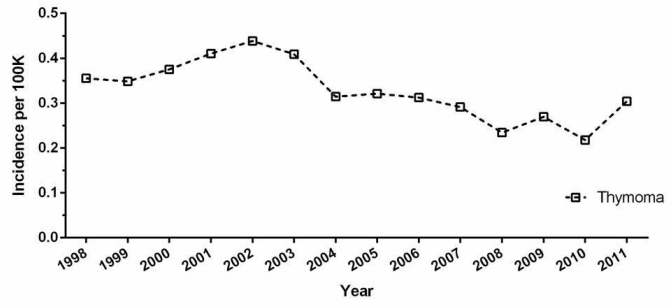


Figure 2. Annual incidence of malignant thymoma in the United States 1998-2011 (per 100,000) in SEER.



Keywords: thymectomy, database, surgery

ORAL 3 - ABSTRACT SESSION 3: REGIONAL TRENDS

ORAL3.04: THE EXTENT OF LYMPH NODE DISSECTION IN THYMIC MALIGNANCIES

ORAL 3 - ABSTRACT SESSION 3: REGIONAL TRENDS

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Background: The proper extent of lymph node dissection (LND) is unclear in thymic malignancies. We investigated the pattern of lymph node metastasis in thymic malignancies based on new ITMIG proposal for lymph node map for thymic malignancies. **Methods:** We retrospectively reviewed 131 thymic malignancy patients who underwent total thymectomy and LND. New ITMIG/IASLC proposals for nodal map and TNM stage classification for thymic malignancies were used for lymph node grouping and TNM staging. Pattern of node metastasis and clinic-pathologic factors affecting node metastasis were analyzed. **Results:** A total of 1348 lymph nodes were dissected in 131 patients. The mean number of dissected lymph node was 10.3 ± 8.5 (range: 1 - 48). A total of 582 anterior regional (N1) lymph nodes were dissected in 107 (81.7%) patients and 517 (88.8%) nodes were peri-thymic, prevascular nodes and lower anterior cervical nodes. A total of 766 deep regional (N2) nodes were dissected in 83 (63.4%) patients. The right paratracheal lymph nodes were dissected in consist 63.4% (486/766) of N2 nodes. Node metastasis was detected in 13 (N1 – 6, N2 - 7) patients. (Table 1.) Six patients had metastasis at peri-thymic lymph nodes and 2 patients had metastasis at the prevascular lymph nodes. Six (86%) N2 patients had right paratracheal nodes (RPN) metastases. Node metastasis rates were 1% in T1 and 37.5% in T2/3. (p < 0.001) Node metastasis rates were 8% in M0 and 43% in M1. (p = 0.03) Node metastasis rate was higher in thymic carcinoma (25%) than thymoma (5.1%). (p = 0.01) Node metastasis rates between subtypes of thymoma were also different. There was no node metastasis in A, AB and B1 types. Tumor size was also significant factor for node metastasis. The optimal cut-off value for the node metastasis was 6cm and the specificity was 62%. Only 16% of patients got preoperative histologic diagnosis. The specificity for the prediction of node metastasis was 100% when T and M stages are combined. (Stage ≥ II) Freedom from recurrence rate of pN1/2 was significantly worse than pN0. (5-year: 38.5% vs 87.9%, p < 0.001) **Conclusion:** Routine en bloc dissection of peri-thymic lymph nodes is recommended during thymic malignancy surgery and the right paratracheal lymph node should be dissected in thymic malignancies ≥ stage II.

Table 1. Patients with lymph node metastasis

	Size (cm)	Type	T	N	M	Metastatic nodes
1	11	B2	3	1	1a	Prevascular
2	8	B3	1	1	1a	Peri-thymic
3	6	C	3	1	0	Peri-thymic
4	6	C	3	1	0	Peri-thymic
5	6.5	C	3	1	0	Prevascular
6	10	C	3	1	0	Peri-thymic
7	9	B2	3	2	0	Right paratracheal
8	9.9	B2	3	2	0	Right internal mammary, Right hilar
9	19	B3	2	2	0	Right paratracheal
10	3.5	C	3	2	0	Right paratracheal
11	5.8	C	3	2	1a	Peri-thymic, Right paratracheal
12	8.5	C	3	2	0	Peri-thymic, Right paratracheal
13	13	C	3	2	0	Right paratracheal, Subcarinal

Keywords: Lymph node dissection, Lymph node metastasis, Thymic malignancy

ORAL 4 - ABSTRACT SESSION 4: PATIENT EVALUATION

ORAL 4 - ABSTRACT SESSION 4: PATIENT EVALUATION

ORAL4.01: COMPARISON BETWEEN CT AND MRI IN PREOPERATIVE EVALUATION OF THYMIC EPITHELIAL TUMORS

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Purpose: Contrast enhanced computed tomography (CT) is currently the imaging modality of choice for distinguishing thymic epithelial tumors (TET) from other anterior mediastinal masses, characterizing the primary tumor and staging disease. Currently the role of Magnetic Resonance Imaging (MRI) in imaging TETS is limited to patients who cannot receive iodinated contrast material. The study's main objective is to assess if chest MRI is as accurate as CT in staging TETs. The second objective is to see if newer shorter MRI sequences can replace conventional MRI sequences without loss of accuracy, leading to a short MRI study. **Materials and Methods:** After IRB approval and patients' informed consent, we prospectively reviewed CT and MRI studies obtained within 30 days prior to surgery in 20 patients with biopsy proven TET. CT was performed with intravenous contrast. Conventional MRI sequences included were SE T1 and FSET2 weighted as well as novel faster sequences (Fast Gradient-echo T1-weighted in-phase and opposed-phase, 3D LAVA, and fast spin echo triple echo Dixon [FTED] T2 weighted). Each patient had an MRI cine sniff test as well as fluoroscopic sniff test for assessment of the phrenic nerve function. Conventional MRI sequences, Fast MRI sequences and CT scans were interpreted by three separate experiences chest radiologists who were blinded to each other's studies and prior imaging studies. Both methods were compared and correlated with Masaoka-Koga staging. Local mediastinal involvement, invasion of phrenic nerve, pleura, lung and vessels was assessed. Sensitivity, specificity and accuracy of each imaging method were compared to surgical pathology (Table). **Results:** Among the study patients, 17 had thymoma and 3 thymic carcinoma, 12 patients had advanced disease (stage III/IV). Sensitivity (100%) was identical for all three imaging methods studies when assessing advanced stage disease but CT and new MRI sequences demonstrated a higher specificity (63%) and accuracy (85%) when compared with conventional MRI sequences (respectively, 50% and 80%). CT more accurately identified local mediastinal involvement (94%) compared with conventional and fast MRI sequences (76%). All imaging methods were similar in the assessment of phrenic nerve, vascular and lung involvement. **Conclusion:** The performance of MRI is similar to that of CT in identifying patients with advanced stage TET. Since patients with advanced disease are usually treated with neoadjuvant therapy prior to surgery, MRI can replace CT in their initial evaluation as well as following neoadjuvant therapy prior to surgery thus decreasing cumulative radiation dose.

Table 1: Sensitivity, specificity, accuracy of imaging modalities

	CT			MRI New			MRI Old		
	Sensitivity	Specificity	Accuracy	Sensitivity	Specificity	Accuracy	Sensitivity	Specificity	Accuracy
Staging	100.00	62.50	85.00	100.00	62.50	85.00	100.00	50.00	80.00
Local Mediastinal Involvement	94.12	0.00	84.21	76.47	0.00	68.42	76.47	0.00	68.42
Phrenic Nerve Involvement	16.67	92.31	68.42	16.67	85.71	65.00	0.00	85.71	60.00
Vascular Involvement	0.00	89.47	85.00	0.00	94.74	90.00	0.00	94.74	90.00
Pleural Involvement	81.82	88.89	85.00	63.64	88.89	75.00	72.73	88.89	80.00
Lung Involvement	66.67	85.71	80.00	66.67	71.43	70.00	50.00	78.57	70.00

Keywords: Thymic Epithelial Tumors (TET), Computed Tomography (CT), Magnetic Resonance Imaging (MRI)

ORAL 4 - ABSTRACT SESSION 4: PATIENT EVALUATION

ORAL4.02: DYNAMIC CONTRAST-ENHANCED MR IMAGING IN RISK STRATIFICATION OF THYMIC EPITHELIAL TUMORS

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Objective: To evaluate the diagnostic performance of dynamic contrast-enhanced MR imaging (DCE-MRI) in risk stratification of thymic epithelial tumors. Methods Ninety-three patients with suspected thymic masses were prospectively included in the study to undergo DCE-MRI prior to surgery or biopsy. The time-intensity curves (TICs) were categorized with type I (with a slow, continuous increase), type II (with a plateau form), and type III (with a gradual decrease). The semi-quantitative parameters, including relative enhancement, maximum enhancement (ME), maximum relative enhancement, time-of-arrival, time-to-peak (TTP), wash-in rate, wash-out rate, and brevity of enhancement, were analyzed among the tumors. **Results:** Thirty-eight low-risk thymomas, 34 high-risk thymomas, and 21 thymic carcinomas were revealed pathologically. Type II TICs were predominantly observed in high-risk thymomas (85.3%) and thymic carcinomas (100%), while type III TICs was mainly seen in low-risk thymomas (57.9%), (p = 0.000). The mean RE of thymic carcinomas (190.35% ± 94.3%) was higher than that of high-risk thymomas (136.5% ± 55.7%) (p = 0.044). The mean MEs of thymic carcinomas (1236.1% ± 389.1%) and low-risk thymomas (1169.1% ± 489.9%) were significantly higher than that of high-risk thymomas (928.2% ± 314.1%) (p = 0.012), respectively. The mean MRE of thymic carcinomas (228.1% ± 99.5%) was higher than those of high-risk thymomas (163.4% ± 56.7%) (p = 0.016). The TTP of low-risk thymomas (126.9 ± 54.8 l/s) was the earliest , then were those of high-risk thymomas (170.6 ± 48.2 l/s) and thymic carcinomas (185.9 ± 33.3 l/s) (p = 0.000). The WIR of low-risk thymomas (45.2 ± 30.7 l/s) was the fastest, then were those of thymic carcinomas (35.6 ± 17.5 l/s) and high-risk thymomas (25.4 ± 8.3 l/s) (p = 0.001). The cutoff RE and MRE to differentiate high-risk thymomas from thymic carcinomas were 154.1% [sensitivity, 69.4%; specificity, 78.9%; and AUC, 0.680) and 175.2% (sensitivity, 76.2%; specificity, 61.1%, and AUC, 0.688), respectively. The cutoff ME to differentiate high-risk thymomas from thymic carcinomas and low-risk thymomas were 951.6% (sensitivity, 81.0%; specificity, 51.4%, and AUC, 0.661). **Conclusion:** According to the type of TICs and dynamic indices, DCE-MRI is of value in predicting low-risk thymomas, high-risk thymomas, and thymic carcinomas.Objective To evaluate the diagnostic performance of dynamic contrast-enhanced MR imaging (DCE-MRI) in risk stratification of thymic epithelial tumors.

Keywords: Dynamic contrast-enhanced MR imaging, thymic epithelial tumors, Stratification

ORAL 4 - ABSTRACT SESSION 4: PATIENT EVALUATION

ORAL4.03: NEEDS ASSESSMENT AND DESIGN OF THE FIRST THYMIC MALIGNANCY AND MYASTHENIA GRAVIS PROGRAM

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Background: Myasthenia gravis (MG) is the most common disorder of neuromuscular transmission, and approximately 15% of

patients with MG develop thymic malignancies (TM), most often thymoma. Patients with MG range from healthy outpatients requiring little intervention to those requiring intensive-care level hospitalization. Similarly, there is a wide range of care required for TM patients, with surgical resection performed in most, and more advanced cases also requiring chemotherapy and/or radiotherapy. Although MG and TM are highly linked, to our knowledge, there have been no multidisciplinary programs developed to provide coordinated care for these medically complex patients. This study was performed to define the needs of MG and TM patients and, in doing so, design the first high-quality, efficient multidisciplinary program. **Methods:** A cohort was identified retrospectively as all patients seen and treated for a primary diagnosis of MG and/or a TM at the University of Pennsylvania between 01/01/2005 and 04/30/2015. Demographics were assessed, along with subspecialties consulted for these patients. Hospital admissions data were analyzed for each patient by calendar year, and included hospitalizations with a primary encounter code frequency of >2%. **Results:** A total of 1,236 consecutive patients were identified, including 881 with MG, 312 with TM, with 43 carrying both diagnoses. Age was distributed in MG and TM, respectively was: 18-39 yo (19, 16%), 40-60 yo (31, 38%), and >60 yo (50, 46%). The majority of patients in both cohorts were Caucasian (67, 68%) or black (15, 17%). The most common subspecialties consulted were neurology (79%), thoracic surgery (13%), and ophthalmology (8%) for MG patients, and were thoracic surgery (65; 84%), radiation Oncology (42; 51%), and medical Oncology (27; 30%) for TM patients and TM and MG patients, respectively. A total of 103 MG patients (12%) underwent plasmapheresis. Hospital admissions averaged 3% and 5%/year for MG and TM patients, respectively, with a total of 36% admitted at least once over the study period. The primary reasons for admission were MG (46%), TM (38%), chest pain or respiratory failure (6%), rehabilitation (5%), chemotherapy (3%), or sepsis (2%). Average length of stay was 7.1 days. **Conclusions:** We have identified a critical need for multidisciplinary programs at tertiary care centers for MG and TM patients, with neurology, ophthalmology, thoracic surgery, radiation Oncology, and medical Oncology identified as the essential subspecialties. There is a relatively high rate of hospital admissions for MG patients, even those not admitted for planned resection of a TM, indicating the need for more intensive and coordinated outpatient management. A novel Myasthenia Gravis and Thymoma Program has been established at our institution. Further studies will be needed to assess its utility with the following endpoints: increasing convenience for providers and patients, optimizing care coordination, shortening diagnosis to treatment time, and reducing hospital admissions.

Keywords: thymoma; myasthenia gravis; program development; radiation; hospitalization

ORAL 4 - ABSTRACT SESSION 4: PATIENT EVALUATION

ORAL4.04: EMERGENCY PRESENTATION OF MEDIASTINAL TUMORS: A CLINICOPATHOLOGICAL STUDY

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Introduction Most of the mediastinal tumors in adults present incidentally or with subtle symptoms like chest discomfort, chest pain, exertion dyspnea, or simply shortness of breath. Little is known about the emergency presentation of such tumors. **Aim of the study** The aim of this study is to evaluate the clinicopathological characteristics of patients with mediastinal tumors who presents acutely to emergency department in a tertiary cancer care center. **Methods** A retrospective review of a prospectively collected database of mediastinal tumors from 2009 till 2015 was analyzed. Demographic data, mode of presentation, presenting symptoms, tumor characteristics, diagnostic procedures, and histology were reported. Data is presented as percentage, mean, and range. **Results** Over the study period, a total of 244 cases of mediastinal mass were collected in the database. 18 cases (7%) presented acutely to the emergency department. There were 12 males and 5 females. Two females were pregnant and presented in third trimester. Age ranges from 25 – 72 years with mean age of 58. The main presenting symptoms included: Stridor (45%), Superior vena cava syndrome (22%), Hypotension (11%), tachyarrhythmia (16%), collapse outside the hospital (6%). The diagnosis was established by mediastinoscopy (33%), Chamberlain procedure (44%), incisional biopsy from non mediastinal site (17%), and Right thoracotomy (6%). One patient presented with stridor and huge posterior mediastinal goiter immediately taken to the operation and the tumor completely resected by a right thoracotomy approach. Due to critical presentation, most patients (61%) had the diagnostic procedure under local anesthesia while awake and the patient is semirecumbent position. All of the mediastinoscopy cases were done under GA in supine position. CT guided biopsy procedure was not used in any patient because either the patient is unstable to go to the radiology suite or the tumor is technically not amenable for such procedure. The anatomic location of these tumors included: Anterior Mediastinum (88%), middle Mediastinum (6%), and posterior mediastinum (6) The tumor size ranges from 7 – 29 cm with a mean of 18 cm. The final pathological diagnosis included: Lymphoma (44%), mesenchymal tumors (6%), thymoma (33%), thymic carcinoma (11%), and benign multinodular goiter (6%). **Conclusion** A small, but clinically important, percentage of patients with mediastinal tumors present acutely to the emergency department. Physicians have a wide array of diagnostic procedures that can be safely utilized to diagnose such tumors. Local anesthesia-based procedures can be safely performed to obtain enough tissue for diagnosis. Clinically, these tumors tend to be malignant and larger than the usually incidentally found counterparts, and mainly in the anterior compartment.

Keywords: Mediastinal, Neoplams, Emergency, Clinical

POSTER SESSION

P01: LONG-TERM SURVIVAL AFTER SURGICAL TREATMENT OF THYMIC CARCINOMA

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Objectives: Thymic carcinoma is a type of highly malignant tumor that originates from the thymic epithelium. It is rare and distinct from thymoma. Treatment methods and prognosis of thymic carcinoma remain controversial. To date, three studies with relatively large sample populations have been conducted based respectively on the Surveillance, Epidemiology and End Results database in the United States, the European Society of Thoracic Surgeons, and the Japanese multicenter database. This paper retrospectively analyzes survival data from a large-sample multicenter database in China. **Methods:** The Chinese Alliance for Research of Thymoma (ChART) constructed a retrospective database of patients with thymic epithelial tumors, which enrolled 2,421 patients from January 1992 to December 2013, including 364 with thymic carcinomas. In this study, we analyzed clinical, pathologic and treatment information, measured long-term survival rates, and identified relevant prognostic factors. **Results:** Of 364 patients, R0 resection was performed in 235 cases (64.6%), R1 in 42 cases (11.5%), and R2 in 87 cases (23.9%). The 3-, 5-, and 10-year survival rates were 79.8%, 69.0%, and 48.5%, respectively. The survival rates of the patients at different Masaoka-Koga stages were significantly different ($P < 0.001$). The survival rate of the patients who underwent complete resection (R0) was higher than that with incomplete resection (R1/R2), and the difference was statistically significant ($P < 0.001$). Postoperative chemotherapy did not significantly affect patient survival ($P = 0.808$). Postoperative radiotherapy significantly improved the overall survival not only of the patients with R1/R2 resection but also of those with stage III/IV disease who underwent R0 resection ($P = 0.003$). Multivariate analyses showed that R0 resection, postoperative radiotherapy and Masaoka-Koga Stage were major prognostic factors of thymic carcinoma. **Conclusions:** Complete resection is the preferred primary treatment for thymic carcinoma. R0 resection, early Masaoka-Koga stage and postoperative radiotherapy are significant predictors of improved survival.

Keywords: Thymic tumors, thymic carcinoma, Staging, Prognostic factors

P02: COMPARISON A NOVEL 3-HOLE SURGERY WITH VATS FOR MYASTHENIA GRAVIS: A RETROSPECTIVE STUDY

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Objective: To compare the safety and effectiveness of a novel 3-hole surgical method using an approach through the subxiphoid with VATS in treating myasthenia gravis. **Methods:** From January 2013 to August 2014, 70 cases of myasthenia gravis were selected, 34 of which were operated on using the novel 3-hole surgical method extended thymectomy approach and 36 using VATS from the right side of the chest. The novel 3-hole surgical method procedure was as follows: 1) With the patient in a supine position and legs apart at 45°~60°, one 2.0-cm incision and two 0.5-cm surgery holes were made subxiphoid and the bilateral rib arch . 2) The retrosternal space was exposed using both blunt and sharp dissection (Fig 1d). The thymus, the bilateral mediastinal pleurae and its surrounding fat tissues were completely removed . 3) At the end of the surgery, drainage was not necessary after draw off all mediastinum CO2. The observed indices were operation time, bleeding volume, length of postoperative hospital stay, occurrence of pain, sternotomy conversion ratio and its reasons, mortality rate from complications. **Results:** 1) The mean surgery time in the 3-hole group was significantly less than that of the VATS group (90.3 ± 21.1 min vs 120 ± 24.6 min, $P < 0.01$), and the volume of bleeding in the 3-hold group was less than that in the VATS group (20.3 ± 8.9 mL vs 55.1 ± 10.4 mL, $P < 0.05$). 2) Among those in the 3-hole group, sternotomy was performed on two cases (5.8% of the total cases) because of the close adhesion of lesions with the left innominate vein. Among those in the VATS group, thoracotomy was performed on four cases (11.1%) because of the close adhesion of lesions with the left innominate vein (5.5%, two cases) and hemorrhage caused by injury to the left innominate vein (5.5%, two cases). There were no differences observed between the two groups (5.8% vs 11.11%, $P = 0.435$). 3) Using the Visual Analog Pain Scale, postoperative pain was assessed as being much lower in the 3-hole group than in the VATS group (3.2 ± 0.8 vs 4.5 ± 1.5, $P < 0.01$). 4) The length of postoperative hospital stay in the 3-hole group was also less than that of the VATS group (2.3 ± 1.1 vs 7.4 ± 2.3 d, $P<0.05$). 5) In both groups, the complication and mortality rates were 0%. **Conclusions:** Our innovative 3-hole surgical method is markedly better than VATS in extended thymus resection in the following ways: 1) Less possibility of injuring any vessels during surgery. 2) The surgery time and bleeding volume were also significantly reduced. 3) Postoperative pain was significantly reduced. 4) Postoperative drainage was not necessary. 5) Postoperative complications and length of stay were also significantly decreased. 6) Bilateral mediastinal pleurae and adipose tissues could be completely removed and the remission rate of myasthenia gravis greatly improved. This is a good surgical treatment for myasthenia gravis.

Keywords: safety, effectiveness, 3-hole approach and VATS, myasthenia gravis

P03: THYMIC NEUROENDOCRINE TUMORS: ANALYSIS OF FACTORS AFFECTING SURVIVAL

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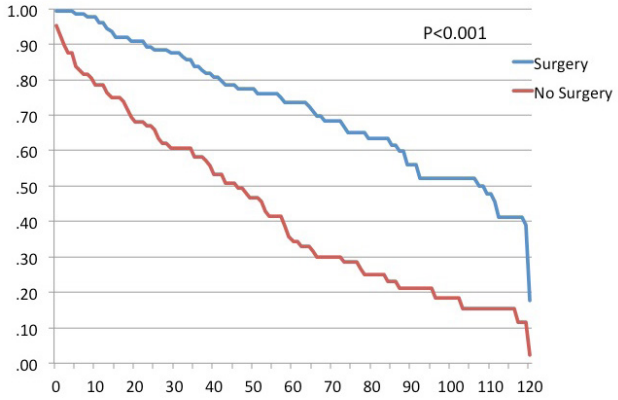
Objectives: Thymic neuroendocrine tumors (NETT) are very rare tumors. This study was designed to identify factors affecting survival including the impact of surgical resection. **Methods:** We queried the Surveillance, Epidemiology and End Results database for all patients diagnosed with NETT from 1988 to 2011. We excluded patients diagnosed at autopsy. Variables significantly affecting survival in univariate analysis were included in a multivariate analysis. **Results:** We identified 254 patients with NETT. Median overall survival was 73 months, and 10-year survival was 71%. Multivariate analysis demonstrated that female sex, lower Masaoka-Koga stage, and surgical resection were significant factors affecting survival. Surgery was performed in 139/254 (54.7%) patients. The majority, 131/139 (94.2%) had resection of the tumor, 8/139 (5.8%) had debulking. There were no significant differences between patients undergoing surgery and those not, except for higher Masaoka-Koga stage among patients not undergoing surgery ($p=0.018$). Median survival in patients who underwent surgery was 109 months compared to 46 months in patients who did not undergo surgery ($p<0.001$, Figure 1). In patients who underwent surgery, 69/139 (49.6%) had nodal sampling and 38/69 (55.1%) had positive nodal metastases. Multivariate analysis demonstrated that MK stage and positive nodal metastases were the only factors impacting overall

survival. Postoperative radiation therapy did not affect survival. Conclusions: In patients with NETT, surgical resection, MK stage, and female sex are important factors impacting survival. In patients submitted to surgery, MK stage and nodal sampling significantly impacted survival. In this rare disease, surgical therapy appears to be the intervention of choice.



Keywords: SEER, Thymic neuroendocrine tumors

P04: ELEVATED SERUM LDH LEVEL PREDICTS BOTH POOR OS AND SHORT RFS AFTER RESECTION OF THYMIC CARCINOMA

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Background: The predictors of overall survival and recurrence-free survival for thymic carcinoma have not been well clarified. The prognostic significant of serum lactate dehydrogenase (LDH) level in thymic carcinoma remains unclear. So we evaluated the role of pretreatment serum LDH level in the prognosis for thymic carcinoma in this study. **Methods:** Sixty consecutive surgical patients were enrolled in this study with pathologic confirmed thymic carcinoma in Sun Yat-sen University Cancer Center from June 1996 to June 2014. Clinical and pathologic data were retrospectively reviewed. Pretreatment serum LDH level was tested. Categorical variables were compared using the Chi-square test or Fisher's exact test. Survival time was analyzed using the Kaplan–Meier method and log-rank test. Multivariate analysis was performed using the Cox proportional hazard model. **Results:** The mean (±SD) pretreatment serum LDH level for this cohort were 214.12 ±107.85. The overall 1- 3-, 5-, and 10-year survival rate was 88.2, 75.4, 66.1, and 62.8%, respectively. The 1- 3-, 5-, and 10-year recurrence-free survival (RFS) rate was 78.3, 58.6, 47.6, and 34.8%, respectively. In both univariate analysis and multivariable analysis, only pretreatment serum LDH level (hazard ratio = 2.749, p = 0.027) and pathological Masaoka stage (hazard ratio = 2.931, p = 0.041) were associated with overall survival (OS). In univariate analysis, pretreatment serum LDH level (p = 0.004), tumor size (p = 0.019), completeness of resection (p = 0.010), postoperative radiotherapy (p = 0.003) and pathological Masaoka stage (p = 0.010) were associated with RFS. Multivariable analysis showed that pretreatment serum LDH level (hazard ratio = 2.696, p = 0.006), postoperative radiotherapy (hazard ratio = 2.922, p = 0.006) and pathological Masaoka stage (hazard ratio = 2.768, p = 0.036) were independently prognostic factors of RFS. This study also found that male patients and larger tumor size had a significantly higher rate of elevated pretreatment serum LDH level than in the other groups. **Conclusions:** Pretreatment serum LDH level is an independent prognosis factor of overall survival and recurrence-free survival, and could be a supplement for Masaoka stage.

Keywords: thymic carcinoma, lactate dehydrogenase, prognostic factor, survival

P05: LOW-DOSE RADIOTHERAPY FOR THE TREATMENT OF PLEURAL RECURRENCE OF THYMIC CARCINOMA

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Background: Pleural recurrence is a common type of failure in some late-staged thymic carcinomas even after primary mediastinal mass is completely removed or well controlled. Generally, systemic chemotherapy would be firstly chosen by most oncologists. But it becomes challenging when chemotherapy shows no efficacy or the tumor relapses after response. In most cases, this group of patients has received high-dose radiotherapy to the mediastinal tumor bed before the pleural recurrence is confirmed. Due to normal tissue (lung, heart et.al.) dose restriction, high dose radiotherapy to the pleural lesions would be highly risky. From Nov 2011, we started trying low-dose intensity modulated radiotherapy (IMRT) as a palliative treatment to these patients. **Methods:** Patients included in this trial should meet the following criteria: 1) pathologically diagnosed thymic carcinoma; 2) primary mediastinal tumor was resected or well controlled by other means; 3) new pleural lesions were detected during the follow-up; 4) chemotherapy failed or tumor relapsed after response; 5) adequate pulmonary and cardiac function. The radiotherapy was conducted using IMRT technique and the dose was prescribed below 40Gy. The gross tumor volume (GTV) should cover all visible lesions. **Results:** From Nov 201 1 to Feb 2015, there have been 14 patients (male: female=9:5) included in this study. The pathological subtype distribution is squamous carcinoma in 12 patients, lymphoepithelioa-like carcinoma in 1 and thyroid carcinoma showing thymus-like differentiation (CASTLE) in 1. According to Masaoka staging definition, three, seven and four patients are classified as stage III, IVa and IVb respectively when initially diagnosed. Surgery was conducted as first-line treatment in twelve patients to macroscopically remove their intrathoracic tumors, and another 2 patients received chemoradiotherapy to control mediastinal tumors. The median time between the first-line treatment and pleural recurrence is 18 (7-55) months. There are 2 patients who received 3 times of IMRT for the recurrence on the different parts of the pleura. There are also 3 patients who received 2 times. Totally there are 21 courses of IMRT completed in this study. The median dose is 30 (20-40)Gy. The median tumor volume is 27 (8-190)ml. The response rate is 100% (CR:PR=11:10). No tumor progression inside the radiation field is discovered until now. The median local control time is 10 (4-44) months. There are 2 patients who developed grade 3 pneumonitis induced by radiation. Another 58-year-old male patient died of grade 5 pneumonitis because he suffered a right phrenic nerve injury in the surgery which resulted in the lifting of right diaphragm and increased the proportion of lung volume exposing to X-ray. **Conclusions:** IMRT showed excellent local control effect in the management of pleural recurrence of thymic carcinoma even with a dose as low as 20Gy. At the same time, the in-field progression free survival time is also encouraging. But for cases with phrenic nerve injury, the potential high risk should not be neglected.

Keywords: thymic carcinoma, pleural recurrence, radiotherapy

P06: A NEW SURGICAL METHOD FOR ANTERIOR MEDIASTINUM TUMORS: A 3-HOLE APPROACH

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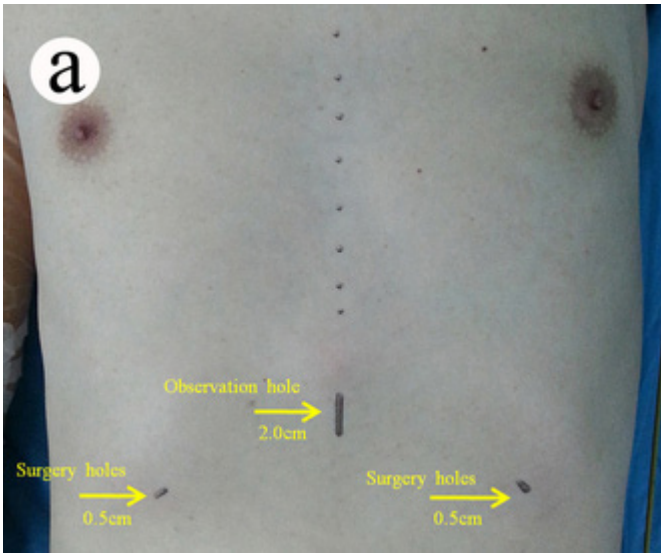
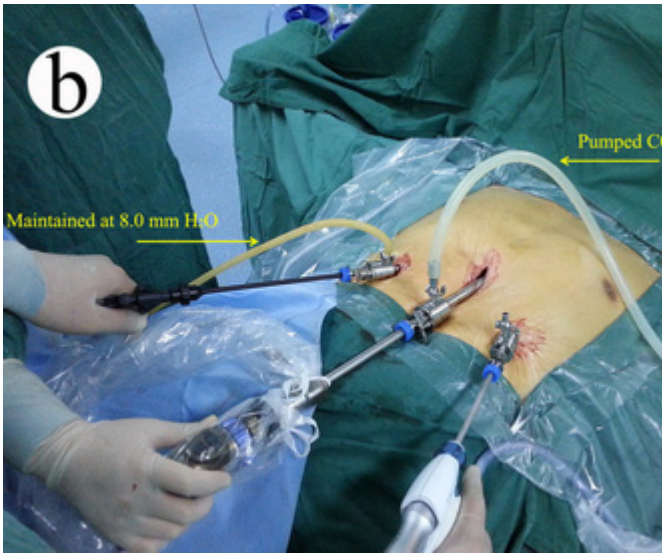
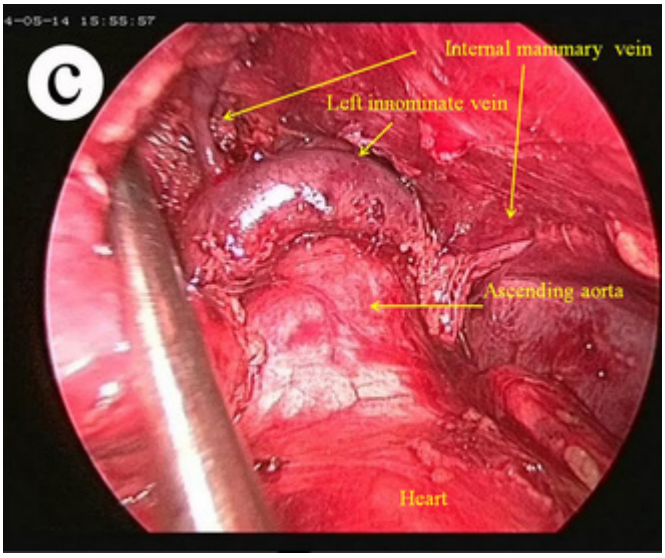
Objective: This study was to introduce a new surgical method for resecting anterior mediastinum tumors through a subxiphoid incision, which accurately combines the advantages of both video-assisted thoracic surgery and standard sternotomy for a minimally-invasive procedure with fewer complications. **Methods:** From January to August 2014, 58 patients underwent surgery using this new method, 34 of whom had myasthenia gravis and had an extended thymectomy. The following surgical procedures were used: 1) With the patient in a supine position and legs apart at 45°~60°, a 2.0-cm incision was made below the xiphoid process to be used as the observation hole. Two 0.5-cm surgery holes were made along the bilateral rib arch at the midclavicular line, and two trocars were inserted into these holes using B-ultrasound guidance. Carbon dioxide (CO2) was pumped into the anterior mediastinum, the pressure was maintained at 8.0 mmH2O, and an ultrasound scalpel and a grasping forceps were inserted through the two surgery holes (Fig 1a,b). 2) The retrosternal space, including the bilateral lower poles of thymus, internal mammary arteries, and phrenic nerves, were exposed using both blunt and sharp dissection. The thymus and its surrounding fat tissue were separated and the thymic veins were severed using an ultrasound scalpel. 3) For myasthenia gravis patients, the bilateral mediastinal pleurae and the affected adipose tissues (around the lower pole of thyroid, left innominate vein, aortic window, sulci venae cavae cranialis of the ascending aorta and bilateral phrenic nerves, and so on) were completely removed. During the entire procedure, the innominate vein, bilateral phrenic nerves, vagus nerves, and left recurrent laryngeal nerve were protected from injury (Fig 1c). 4) At the end of the surgery, the lungs were dilated to exhaust the CO2 and a latex tube was inserted through the observation hole to draw off all gas in the mediastinum. Drainage was not necessary.







Results: The mean bleeding volume was 20 mL, the mean surgery time was 90 min, and the average postoperative hospital stay was 2 d. There were two cases (3.45% of the total) of sternotomy that were necessary because the affected sites could not be freed from the left innominate vein. No massive hemorrhage occurred in any of the cases. The postoperative mortality rate was 0, and no recurrence was observed in follow up. **Conclusions:** This new 3-hole surgical method combines the effectiveness and safety of a standard sternotomy with the minimal invasion and quick recovery of thoracoscopy. It can also thoroughly remove the affected sites using accurate and controllable steps with less postoperative pain, fewer complications, less economic burden, shorter postoperative hospital stay.

Keywords: anterior mediastinum tumors, new surgical method, 3-hole approach

P07: EFFECTIVENESS OF CYTOTOXIC AGENT ETOPOSIDE AFTER TARGET THERAPY IN ADVANCED THYMIC TUMORS

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Background We describe three cases of thymic epithelial tumors

(TET) heavily pretreated, which responded to oral etoposide, after progression to Everolimus. **Methods** The first patient is a 50-years old woman with a diagnosis of squamous thymic carcinoma from April 2006, judged inoperable. The second patient is a 51-years old woman, with diagnosis of thymoma B2/B3 from June 2004, who progressed after radical surgery. The third patient is a 40-years old man, with diagnosis of functional neuroendocrine thymic carcinoma, discovered for an associated Cushing Syndrome ACTH dependent, went to no radical surgery. All of them had TET stage IVB sec. Masaoka-Koga. A first line platinum based plus anthracycline chemotherapy was administrated, after they received single agent octreotide LAR as maintenance treatment due to the positivity of Octreoscan. At progression they underwent to a series of other several treatments as: gemcitabine plus capecitabine and everolimus. In the first and third patient everolimus was administrated in association with somatostatin analogs, obtaining respectively a PFS of 31 and 6 months. In the second patient indeed, it was administrated alone, obtaining a PFS of 4 months. After progression, all of them received oral etoposide at dose of 50 mg daily three week on/ one week off. **Results** All the patients showed the best response disease, assessed with a CT scan total body, to oral etoposide as sixth line of systemic therapy, after progressed to everolimus. Specifically, they are still on treatment and the time to progression has not been reached. **Conclusion** Our experience of long lasting management of advanced relapsed TET, can prove how the chemosensitivity in this setting of patients, has been restored after the administration of biological agents. Further studied are needed to investigate the biological modification of TETs due to this sequence of treatment.

P08: SOMATOSTATIN ANALOGS PLUS PREDNISONE IN AGGRESSIVE HISTOTYPE AND ADVANCED STAGE OF TETS

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Background Thymic epithelial tumors (TETs) are rare neoplasms characterized by histological variability and different expression at the molecular level. Several biological agents have been evaluated in TETs in small phase II trials. Efficacy of octreotide/lanreotide with or without prednisone in TETs OctreoScan positive has been widely demonstrated in thymoma, but no clearly in thymic carcinoma. **Methods** Twelve patients (five men, seven women; median age 47 years; range 27-70) with advanced stage disease according to the Masaoka-Koga staging system (seven with IVa stage; five with IVb stage), and aggressive histotype according to WHO classification, revised by central review (two B2/B3; five B3; one B3/thymic carcinoma; four thymic carcinoma) were enrolled in this monocentric referral study. All the patients showed a progressive disease according to RECIST 1.1 criteria to previous conventional chemotherapeutic regimens platinum or not platinum-based. All the patients performed OctreoScan. The schedule includes administration of long-acting analog octreotide (30 mg/every 28 days intramuscularly) plus prednisone 0.2 mg/kg/day until progression of disease was documented. Overall response rate and toxicity were evaluated. **Results** The median time to progression was 6 months (range 3-24), the overall response rate was 74.9%, particularly three patients (25%) obtained stable disease; four patients (33.3%) partial response; two patients (16.6%) complete response; three patients (25%) progression disease. One patient with Good Syndrome interrupted treatment after 6 months for infection disease. One patient has been lost to follow-up after 24 months of treatment. One patient died after progression disease for PRCA. Treatment was generally well tolerated with acceptable toxicity: no symptomatic cholelithiasis (1 patient), Grade 1 diarrhea (two patients) hyperglycemia (1 patient). One patient with thymic carcinoma and IV b stage had PS improvement from 2 to 1 sec ECOG, and one patient had complete remission of pericardial and pleural effusion after six months treatment with symptomatic relief. **Conclusion** These results show that the association of somatostatin analogs plus prednisone is an effective treatment in aggressive histotype and advanced stage disease of TETs.

P09: DIAGNOSIS OF ADVANCED THYMIC EPITHELIAL TUMORS IN PATIENTS PREVIOUSLY AFFECTED BY THYMIC HYPERPLASIA

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Background Thymic hyperplasia is a rare differential diagnosis of anterior mediastinal lesions. Histological and radiological criteria are used to distinguish this benign condition from other malignant diseases; it is often associated with Myasthenia gravis. Here we report our monocentric experience of five patients, affected by advanced thymic epithelial tumors, with a previous diagnosis of thymic hyperplasia. **Methods** Four patients (two female and two male with a median age of 61 years, range 52-71), went to Referance Rare tumors centre of Naples from September 2013 to July 2015, had a previous history of thymic hyperplasia. All patients were affected by Myasthenia Gravis in the young age and for this reason they underwent to radical thymectomy in 1994 in our thoracic surgery department. The diagnosis was confirmed histologically. All of them, after twenty years, received the diagnosis of advanced thymic epithelial tumor, specifically one patient at stage of disease IV A sec. Masaoka-Koga and B2 histotype sec. WHO 2004, three patients at stage IVB and B3 histotype. They were candidated to first line platinum based chemotherapy, only one patient underwent to radical surgery and adjuvant chemotherapy. **Results** One patient died after two years from diagnosis because of septic shock, two patients have a stable disease and one patient is still on treatment. **Conclusion** Here we report this experience to underline the importance of a previous diagnosis of thymic hyperplasia. It may be considered as a risk factor for the development of a more aggressive and extended disease due to a possible carcinogenesis model. Further studies are needed.

P10: IS THE OCTREOSCAN SCORE A PREDICTIVE FACTOR OF RESPONSE TO SOMATOSTATIN ANALOGS TREATMENT?

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Background The somatostatin receptor expression in thymic neoplasms is assessed in vivo imaging by 111In-octreotide SPECT (Octreoscan). This retrospective study aimed to verify the predictive role of intensity expression of Octreoscan to somatostatin analogues treatment. **Methods** We evaluated 28 patients (fourteen male and fourteen female with a median age of 54, range 27-78) with thymic tumors candidated to somatostatine analogs therapy as second or third line of treatment or maintenance treatment. For this reason all of them performed Octreoscan of the thorax and tumor-to-background ratio was determined on the 24-hour coronal sections. Thymic tumors were classified by WHO 2004 and staged according to Masaoka-Koga system. Specifically, AB 3 pt; B1 2 pts; B2 5 pts; B3 9 pts; B2/B3 3 pts; thymic carcinoma 5 pts; B3/thymic carcinoma 1 pt. All the patients had a III of IV stage of disease. Lesions with pathologically increased tracer uptake were categorized according to the following 3-pointscore: equivocal, probably pathologic, and definitely pathologic. **Results** All patients were

Octreoscan positive, four with an equivocal point score, nineteen and five with a probably and definitely pathological score respectively. Somatostatin analogs were administrated as second or third line of therapy in ten patients, as maintenance therapy in sixteen patients and as both of modality in two patients. Median time to progression was16 months (range 6-77) and it was not influenced by uptake pathological score. **Conclusion** The intensity of uptake of Indium-111-DTPA-D-Phe1-octreotide in thymic tumors is not a predictive factor of response to somatostatin analogues treatment. The Octreoscan positivity is the best rationale for treating thymic epithelial tumors with somatostatin analogs.

P11: 18FDG-PET/CT FOR EARLY PREDICTION OF RESPONSE TO FIRST LINE PLATINUM CHEMOTHERAPY IN ADVANCED TETS

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Background To investigate the value of the metabolic tumor response assessed with 18F-fluorodeoxyglucose positron emission tomography (FDG-PET), compared with clinico-biological markers, to predict the response disease to first line platinum based chemotherapy in advanced thymic epithelial tumors. **Methods** Twenty patients with diagnosis of thymic epithelial tumor and stage of disease III and IV sec. Masaoka-Koga, were retrospectively included in this monocentric study. Different pre-treatment clinical, biological and pathological parameters, including histotype sec. WHO 2004 and stage of disease sec. Masaoka-Koga were assessed. Tumor glucose metabolism at baseline and its change after the first line platinum based chemotherapy (from four to six cycles) were assessed using FDG-PET, moreover the response disease was assessed using total body CT scan for the evaluation of RECIST criteria 1.1. **Results** Twelve patients had an objective response to the first line platinum based chemotherapy according RECIST criteria 1.1 and all of them started with a SUVmax at baseline major than 5, indeed the other eight patients, non-responders to chemotherapy, had a SUV max at baseline minor than 5. **Conclusion** It is important to define the chemosensitivity of advanced thymic epithelial tumors early. Combining bio-pathological parameters with the metabolism at baseline assessed with FDG-PET can help the physician to early predict the probability of obtaining a disease response to first line platinum based chemotherapy. The SUVmax cut off of 5 at 18FDG-PET/CT performed at baseline treatment, might be a new parameter for choosing the most powerful first line of chemotherapy. Given these results, further prospective studies are needed to establish a new first line therapy in advanced thymic epithelial tumors with a low SUVmax at baseline, non responders to conventional chemotherapy.

P12: SOMATOSTATIN ANALOGS AS MAINTENANCE THERAPY IN HEAVILY PRETREATED THYMIC EPITHELIAL TUMORS

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Background Thymic epithelial tumors are rare neoplasms with a particular biological behavior, treated with a combination of therapeutic strategies such as surgery, chemotherapy, radiotherapy and target agents. No continuation maintenance therapy exists for these rare tumors. An high uptake of indium-labeled octreotide (111In-DTPA-D-Phe1-octreotide) and curative application of somatostatin analogs in thymic tumors have been widely demonstrated. **Methods** Eighteen patients (nine women and nine men, median age 54.5 years; range 32-78) with advanced thymic tumors (seven patients with stage III; seven with IVa; Four with IVb according to the Masaoka-Koga staging system), histotype sec. WHO revised by central review (three AB, two B1, three B2, five B3, three B2/B3, two thymic carcinoma) with a partial response or stable disease to conventional chemotherapeutic regimens platinum or not platinum-based, after performed OctreoScan, were enrolled in this monocentric referral center study. The schedule includes administration of long-acting analog octreotide (30 mg/every 28 days intramuscularly), until progression of disease was documented. Median time to progression and toxicity were evaluated. **Results** Median follow-up was of 43 months with a median time to progression of 14,5 months (range 77-2). Treatment was generally well tolerated with acceptable toxicity: Grade 1 diarrhea (5 patients), Grade 2 hyperglycemia (4 patients). No patients interrupted treatment because of toxicity. **Conclusions** The current study indicates that single-agent somatostatin analogs maintenance therapy is a potential treatment strategy for advanced TETs OctreoScan positive which respond to previous conventional chemotherapy. In particular, somatostatin analogs may provide an effective maintenance treatment duration regardless of histotype and stage of disease with an acceptable toxicity and an improved patients' compliance.

Keywords: somatostatin analogs, thymic tumors, Octreoscan

P13: ESTABLISHMENT AND CHARACTRIZATION OF A NOVEL HUMAN THYMOMA CELL LINE

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Background: Thymomas are the most frequent tumors of the anterior part of the mediastinum. However, therapeutic progress is hampered by a deficiency of appropriate pre-clinical models and the complexity of the disease. In this study, we develop a new cell line, designated as T-AB-1, which was established from a patient with World Health Organization-type AB. Objective. To establish a new human thymoma cell line and to provide an experiment model for research on thymoma. Methods. Surgically resected specimen of a case of thymoma of type AB was collected, After primary culture and cloning, a cell line disignated as T-AB-1 was established and its biological features were investigated, including morphology, ultrastructure, growth kinetic features, tumorigenicity to nude mice and expression of epithelial cell markers. Results. Cell lines were considered to be established after 15 passages. Cell lines have maintained an in vitro culture for more than 36 months (3 years). The cell line grew continuously in vitro with a doubling time of 35.2 hours and was passaged over 50 times. The thymoma cells possessed the morphology and structure features of epithelial cells. The cell line showed tumorigenicity to nude mice and the histologic features of the tumors developed were similar to the origin tumor from which the cell line derived. The xenografted tumor exhibited the characteristics of thymoma type AB. The T-AB-1 cell line showed a stronger reaction to epithelial markers (such as pan-cytokeratin, CK8, CK18, CK19 and so on) and weaker reaction to B- and T-cell lineage markers. Conclusion. All findings and evidence in this experimental study suggested that this cell line might be a useful model in vitro in cellular and molecular studies as well as in testing novel therapies for human thymoma.

Keywords: Thymoma; cell line; WHO classification; cell culture; Establishment

P14: FEASIBILITY OF "SUBXIPHOID AND SUBCOSTAL" APPROACH IN VATS THYMECTOMY FOR PATIENTS WITH MG

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Objective To investigate the safety and feasibility of the subxiphoid and subcostal approach in video-assisted thoracoscopic (VATS) extended thymectomy for patients with myasthenia gravis (MG). **Methods** Clinical data of 45 eligible patients who underwent VATS extended thymectomy for MG in our department from April 2014 to June 2015 by the same surgical team were retrospectively analyzed. 25 through right chest cases (Group A), placed in the 30° left lateral decubitus position, were made three 5 to 10mm incisions on the right chest. The en bloc dissection of thymus and perithymic and pericardiophrenic fatty tissue was achieved under the condition of general anesthesia with trachea double catheter insertion and one-lung ventilation. 20 subxiphoid and subcostal cases (Group B), placed in the type supine position, were made a 15mm subxiphoid thoracoscope incision and two 5mm operation incisions at the intersection point of bilateral midclavicular line and subcostal margin and resected the thymus and adipose tissue in the middle of bilateral phrenic nerve under the condition of general anesthesia, with trachea single catheter insertion and artificial pneumothorax. Retrospective analysis the clinical data of the two groups. **Results** All the surgeries were finished successfully without conversion to open thoracotomy. There were no significant differences between the two groups in operation time and the length of postoperative hospital stay.[operation time: Group A(139.5±39.7) minutes, Group B(136.1±51.7) minutes; postoperative hospital stay: Group A(10.2±17.5)d, Group B (3.8±1.1)d; P>0.05]. The amount of blood loss and thoracic drainage periods in Group B were less than Group A.[amount of blood loss: Group A(138.8±123.0)ml, Group B(66.5±42.8)ml; thoracic drainage periods: Group A(1.7±1.0)d, Group B(1.0±0.4)d; P<0.05]. **Conclusion** This procedure offers the advantage of good surgical access for dissection around the bilateral phrenic nerves in extended thymectomy. It is more easily for surgeons to fully reveal the left phrenic nerve and the upper thymic poles.

Keywords: Subxiphoid, Thoracoscopic, Extended thymectomy

P15: THE EXPRESSION OF TC17 CELLS IN THYMOMA ACCOMPANY WITH AUTOIMMUNE DISEASES OR AUTOIMMUNE DISORDERS

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Objective: Thymoma is thymic epithelial cell tumor. Studies have shown that thymoma associated with autoimmune disorders and possible mechanisms of autoimmune diseases is the central immune tolerance and peripheral tolerance obstacles have resulted in the breaking of the autoimmune response activation and immune tolerance. Tc17cells and Th17cells have been shown play an important role in tumor and autoimmune diseases' Development process .This study test the Distribution of Tc17cells in thymoma and the expression of RORγt in thymus of thymoma patients with MG or other autoimmune diseases, the freguency of Th17/Tc17 in PBMCs. To explore The expression of th17/tc17 cells in thymoma accompany with autoimmune diseases or autoimmune disorders. **Methods:** In this study, grouped as follows (1) thymoma non gravis group (Tm groups) (2) thymoma with myasthenia gravis group thymoma with myasthenia gravis (MG group) (3) thymoma with myasthenia gravis associated with other autoimmune diseases group or antinuclear antibodies abnormal elevation of the group (AD group), to analyze the basic differences between the groups. In this study,We examined the RT-PCR to detectRORγt in the thymoma tissue, immunohistochemical Double staining method to detect Tc17cells expression and localization in the thymoma tissue distributionexpression Th17/Tc17 in PBMCs by flow cytometry (Interleukin (IL)-17-producing CD8+cells as Thl7 cells and IL-17-producing CD4+ cells as Tcl7 cells), analysis of differential expression of three in each group thymoma; and explore of Th17/Tc17 expression. **Results:** (1) Tm groups and AD group serum CD8 + cells was statistically significant (P <0.05),Tm groups and MG group serum CD4 + cells / CD8 + cells was statistically significant (P <0.05); Tm and MG /AD group serum, C3 statistically significant (P <0.05);Tm and MG /AD group serum, CRP statistically significant (P <0.05); Tm groups and AD group serum IgE cells was statistically significant (P <0.05) (2) In thymoma tissus, the level of Tc17cells in MG/AD group was significantly higher than that in Tm, was statistically significant (P <0.05); (3) PCR tests RORγt mRNA levels , MG/AD group was significantly higher than that in Tm, statistically significant (P <0.05), according to the Osserman classification was statistically significant (P <0.05); (4) In PBMCs' Th17/Tc17 cells have rise trend in Tm groups and MG/AD group. **Conclusions:** CD8 + cells, CD4 + / CD8 + T ratio, immunoglobulin, CRP and complement C3 levels can be used as indicators of evaluation of the role of the immune status of patients with thymoma; (2) RORγt mRNA is the key factors of Th17/Tcl7 cells differentiation, it may play a important role in thymoma accompany with autoimmune diseases or autoimmune disorders. (3) All these authenticate that Th17/Tcl7 cells are involved in the antitumor immunity and autoimmune disorders, which may offer evidence to a probability of immunotherapy.

Keywords: Thymoma, Tc17, Th7, autoimmune diseases

P16: THE IMPACT OF THYMOMA CELL APOPTOSIS AFTER DOWN WNT4 GENE

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Objective: To explore the impact of thymoma cell apoptosis and the signal pathway that Wnt4 gene works through in thymoma cells after interferring Wnt4 gene by using shRNA. **Methods:** Here we construct four shRNA-Wnt4 interference plasmids Which were directed at Wnt4 gene. The blank plasmid, TR001 plasmid and recombinant plasmids were transfected into thymoma cells. The expression of Wnt4 was detected by RT-PCR meanwhile selected the best Wnt4 interference plasmid for subsequent experiments. The thymoma cells were divided into four groups: control group, lipo2000 group; transfected TR001 plasmid, transfected interference plasmid.The impact of apoptosis after down Wnt4 gene was detected by Wright's-Giemsa's mixed stain, Hoechst-33342 / PI fluorescence stain, flow cytometry and Western blot detection of Caspase-3 and cleavage fragments. At the same time the thymoma cells were divided into three groups:control group, transfected TR001 plasmid, transfected interference plasmid. The expression of Wnt4,JNK and β-catenin were detected by RT-PCR and Western blot. **Results:** We have compared with the corresponding control groups ,The shRNA-Wnt4-3 plasmid is the best Wnt4 interference plasmid for subsequent experiments. The ratio of inhibition was 52.37% (P<0.05). Furthermore, the apoptosis rate was significantly increased in shRNA-Wnt4-3 plasmid group (14.70±0.62 p<0.001). Lastly, when down Wnt4 the expression of JNK was significantly down-regulated in thymoma cells (P<0.01). **Conclusion:** We suggest that the shRNA-Wnt4-3 plasmid which we constructed can significantly interference the expression of Wnt4 gene in thymoma cell. Through interfering Wnt4 gene can promote the apoptosis rate of the human thymoma cell. This appearance indicates that the aberrant expression of Wnt4 gene may be one of the mechanisms of occurrence and development of thymoma. After interference Wnt4 gene by using shRNA, the expression of JNK gene is significantly reduced. This appearance indicates that Wnt4 gene is correlated with the expression of JNK gene in thymoma cells. And this work may depend on the non-canonical Wnt/ JNK signaling pathway.

Keywords: Thymoma, Wnt4

P17: DO ASSOCIATED AUTO-ANTIBODIES INFLUENCE THE OUTCOME OF MYASTHENIA GRAVIS AFTER THYMECTOMY?

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Myasthenia gravis (MG) is a neuromuscular autoimmune disease, where antibodies against the acetylcholine receptor destroy this receptor. The role of thymectomy in the treatment of MG remains controversial. Because of the frequent association with other autoimmune diseases, we hypothesized that patients with multiple autoantibodies (autoAbs) might have a lower chance of reaching complete stable remission after thymectomy. We analyzed sera of 85 MG patients who underwent a thymectomy between April 2004 and December 2012. We used four different immunodot kits (D-Tek, Mons, Belgium): ANA25 Quantrix, Synthetase 10 Diver, Myositis 7 Diver and Liver 10 profile Diver, all automatized on the BlueDiver Instrument (D-Tek). The Myasthenia Gravis Foundation of America (MGFA) postintervention status was used to determine the outcome after thymectomy. AutoAbs other than anti-acetylcholine receptor (AChR) antibodies were detected in 29.4% of the patients of whom 16.5% clinically had a second autoimmune disease. In none of the seronegative patients other autoAbs were detected. No significant difference was observed in the 3-years remission rate after thymectomy in patients with or without antibodies other than anti-AChR antibodies. Although these autoAbs do not predict outcome in our MG patient cohort, screening for multiple autoAbs in MG patients might be warranted to identify patients with additional autoimmune diseases.

Keywords: thymectomy, myasthenia gravis, BlueDiver instrument, auto-antibodies

P18: THORACOSCOPIC COMPLETE THYMECTOMY FOR THYMOMA

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Objective Thymectomy was the standard method for the treatment of thymoma. Video-assisted thoracoscopic (VATS) thymectomy was developed more than 20 years ago and has become a widely accepted surgical approach. We consistently performed 3-port VATS simple thymectomy for thymoma. Our indications for VATS simple thymectomy are thymoma without myasthenia gravis(MG) less than 10 cm in the maximum diameter and positioned below jugular notch of the sternum. Extended surgical procedures are thymectomy with combined resection of internal thoracic artery and vein, lung, pericardium, phrenic nerve and diaphragm. **Methods** We retrospective reviewed 502 patients who underwent surgery for mediastinal tumor or disease in our department between 2005 and 2014. Eighty-eight patients underwent VATS thymectomy for thymoma without MG (We performed VATS extended thymectomy for MG).All procedures were performed under general anesthesia with one-lung ventilation. Patients were placed in the lateral decubitus position and three ports were made. We performed VATS thymectomy using mainly right-sided approach because of easy understanding of the anatomy. Left-sided approach was chosen in cases of suspected invasion for left lung or thoracic organs. We hardly insert chest drain unless lung resection or injury. **Results** The 88 patients (40men, 48women) were mean age of 58±12 years. There were 62 right-sided approaches and 26 left-sided approaches. A total of 75 patients received a simple thymectomy, 5 with combined resection of lung, 4 were of pericardium (2 were of lung and pericardium), and 6 were of other lung diseases. The mean operation time was 140±48min, mean intraoperative blood loss was 71ml, and mean postoperative hospital stay was 3 days. There were no operative death or severe complications, and no conversions to open thoracotomy. The pathologic stage was classified as Masaoka stage1 in 39, stage2 in 46, stage3 in 2 and stage4 in 1. It was also classified as WHO classification A in 12, AB in 30, B1 in 14, B2 in 28 and B3 in 4. The mean tumor diameter was 45.2±23mm (ranging from 13 to 100mm). Recurrence was observed in 2 cases (2.3%) as disseminations. One was 72mm, stage2, type B1, the other was 50mm, stage2, type B2. **Conclusions** VATS thymectomy was safe procedure and can be a curative treatment choice.

Keywords: VATS, Thoracoscopic complete thymectomy

P19: COMBINED TRANSCERVICAL AND BILATERAL-THORACOSCOPIC EXTENDED THYMECTOMY FOR THYMOMA WITH MG

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Background To explore the efficacy of combined transcervical and bilateral-thoracoscopic extended thymectomy approach for myasthenia gravis with thymoma stage I or II. **Methods** From Jan 2014 to present, patients with thymoma with myasthenia gravis were enrolled into this study. All the patients were diagnosed and well prepared by a multidisciplinary team, including neurologists, ICU physicians and surgeons. All the operations were conducted by the same surgical team with the same approach: combined transcervical and bilateral-thoracoscopic extended thymectomy. **Results** A total of 16 patients were recruited. Their mean age was 44 years, nine patients were females, and 6 were males. The patients in Osserman classification were 5 in grade I, 6 in grade II a, 4 in grade II b, and 1 in grade III. The patients in Masaoka classification were 7 in grade I, and 9 in grade II. The disease duration ranged from 0.5 to 84 months. The mean length of surgery was 109 minutes (range, 80 to 140min). Intraoperative blood loss was ranging from 30 to 100ml. No case sustained myasthenic crisis perioperatively. The pathology analysis indicated that subgroup distribution was AB/B1/B2, 5/5/6. Three cases were found to have ectopic thymus in the neck, with pathology proved. During the follow-up, no tumor recurrence was found and 3 cases achieved complete remission during the first year after operation, while for the others remains unclear. **Conclusion** Our primary result suggested the combined transcervical and bilateral-thoracoscopic extended thymectomy approach could achieve a curative resection and good cosmesis in myasthenic patients with stage I or II thymoma.

Table 1. All the Patients Date

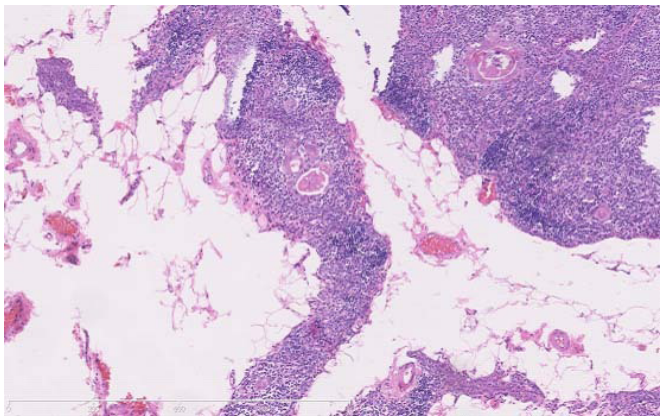
Case	Gender	Age	Osser-man classifi-cation	Pathol-ogy	Masoka classifi-cation	Dura-tion of disease (months)	Preoperative medication
1	F	58	I	AB	I	1	Pyridostigmine, 60mg,tid
2	M	33	IIa	B2	II	7	Pyridostigmine, 60mg,tid
3	M	52	IIa	AB	I	17	Predinisone, 20mg,qd
4	F	27	IIb	B1	II	12	Pyridostigmine, 60mg,id
5	M	52	IIb	B2	II	0.5	Pyridostigmine, 60mg tid
6	F	25	IIb	B2	II	2	Pyridostigmine, 60mg,qid, Predisone, 30mg,gd
7	F	23	I	B1	I	3	Pyridostigmine, 30mg,tid
8	F	20	I	AB	II	2	No
9	M	56	IIa	B2	II	1	No
10	F	46	IIa	B1	II	1	Pyridostigmine, 30mg,tid
11	F	39	IIb	B2	I	84	Pyridostigmine, 30mg,tid
12	M	63	IIa	AB	I	2	Pyridostigmine, 30mg,tid Predi-sone, 20mg,gd
13	M	43	I	B1	I	2	No
14	F	45	III	B2	II	3	No
15	F	56	IIa	B1	II	2	Pyridostigmine, 60mg,tid Predinisone, 20mg,qd IVIG,1 week before surgery
16	M	66	I	AB	I	12	Pyridostigmine, 60mg, tid Predinisone, 20mg,qd

Note: # MG: myasthenia gravis; * IVIG: intravenous immunoglobin

Table 2. Surgical outcome of this group

Variables	Values
Pathology	
AB/B1/B2	5/5/6
Ectopic thymus	
Yes	Case 2,5,11
Cervical/other	3/0
Intraoperative blood loss , ml (range)	67ml (30-100)
Conversion	no
Myasthenia gravis crisis after operation	no
surgical time, min (range)	109 min (80-140)
tumor recurrence	no
Complete remission rate (CSR)	3 cases

Figure Microscopic findings of the etopic thymus tissue found in the cervical region of Case 5



Keywords: thymoma, myasthenia gravis, thymectomy

P20: EXPRESSION AND CLINICAL SIGNIFICANCE OF AUTO-IMMUNE REGULATOR IN THYMOMAS WITH AUTOIMMUNE DISEASE

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Objective: The autoimmune regulator (Aire) is a crucial regulator of autoimmunity in the thymoma. This study is aimed at detecting the expression of Aire in human thymoma with autoimmune diseases and investigating the clinical significance. **Methods:** The expression of Aire in 79 cases of thymoma (Tm) and thymoma with myasthenia gravis (MG)/other autoimmune disease (AD) or not, detected by immunohistochemical SP method. Combined with thymoma and other groups, thymoma Masaoka clinical stage, thymomas WHO histological type, thymoma with myasthenia gravis (MG) /other autoimmune disease or not. The relationship between Aire and clinicalfeatures of thymoma was analyzed. **Results:** The positive rate of Aire in Tm was significant higher than that in MG, the positive rate of Aire in MG was significant higher than that in AD (49% vs 30% vs 12%,P < 0.05). The expression of Aire was associated with thymoma Masaoka clinical stage, thymomas WHO histological type, thymoma with postoperative complications or not (P< 0.05). **Conclusion:** Aire is remarkably correlated with the occurrence, histological type and clinical stage of thymoma. Testing expression of Aire will be helpful for predicting the clinical diagnosis and prognosis of thymoma with autoimmune disease. Tab1.Variable levels of Aire$^+$ cells in the different groups of thymomas.

	Aire$^+$ percentage (%)	P value*
Tm	49±19	0.03
MG	30±11	0.02
AD	12±7	

* P=0.03 Tm vs MG; P=0.02 MG vs AD Tab2.The analysis of Aire expression and clinical characteristics in thymoma patients

	$Aire^+$	$Aire^-$	χ^2	P
Gender			0.339	>0.05
Male	15	21		
Female	29	14		
Age (years)			0.218	>0.05
>50	12	19		
<50	20	28		
Osserman classification			6.216	<0.05
I,IIa	13	10		
IIb,III,IV	17	39		
MASAOKA Stage			6.459	<0.05
I,II	30	12		
III,IV	7	28		
WHO classification			5.768	<0.05
A,AB,B1	27	16		
B2,B3,C	11	25		
Complication			9.876	<0.05
positive	5	11		
negative	33	30		
Admitting days			1.527	>0.05
>25	9	13		
<25	26	31		

Keywords: Thymoma, autoimmune abnormality, autoimmune regulator, clinical significance

P21: TO EXPLORE THE VALUE OF QIANGJI JIANLI METHOD FOR THE MG PATIENTS UNDERWENT EXTENDED THYMECTOMY

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Background Qiangji Jianli capsule or Qiangji Jianli Tang is a drug consisting of some medicinal herb, which has been used in the treatment of MG for many years. Some research suggests this drug can promote the contraction strength of the diaphragm muscle, which plays an important role for the ventilation of lung. Based on this theory we raised the hypothesis that preoperative medication of Qiangji Jianli method may decrease the incidence of postoperative myasthenic crisis. Neutrophil to lymphocyte ratio (NLR) is used as a marker of subclinical inflammation. Some researchers suggested that increased preoperative NLR is associated with poor prognosis of various cancers. **Objective** The purpose of this study is to evaluate that if the preoperative use of Qiangji Jianli method has a meaningful value in the prevention of postoperative myasthenic crisis. We also will explore the dynamic change of the neutrophil to lymphocyte ratio during the perioperative period. **Methods** The detailed clinical data of 44 patients with MG undergoing thymectomy from November 2011 to January 2015 were retrospectively reviewed. Patients were divided into Qiangji Jianli group and routine medication group based on the preoperative medication of Qiangji Jianli Tang or not. Detailed clinical data, for example, the classification of MG, the onset age of MG, history of MG crisis, operative time, percentage of MG crisis, hospital stay length, as well as the preoperative and postoperative NLR was recorded and compared between the Qiangji Jianli group and routine medication group. **Results** There were 44 patients involved in this retrospective study. 24 patients in the Qiangji Jianli group, 20 patients in the routine medication group. The percentage of postoperative MG crisis is 4.16%, 10% respectively, the difference is not statistically significant (P=0.44). The overall percentage of postoperative MG crisis is 6.82%,which is lower than the average percentage of reported literature in the same period. All the patients with postoperative MG crisis required invasive mechanical ventilation and prolonged postoperative hospital stay compared the patient without postoperative MG crisis, (13.33±1.15 vs 6.70±2.37 P=0.00). The postoperative neutrophil to lymphocyte ratio in the Qiangji Jianli group is higher than the routine medication group (13.46±7.59 vs 8.41±5.39,P= 0.02). **Conclusion** Preoperative medication of Qiangji Jianli can greatly decrease the incidence of postoperative myasthenic crisis, in the term of myasthenic crisis, because the limited number of our sample, the difference between the two groups is not statistically significant. The high level of postoperative neutrophil to lymphocyte ratio has a good correlation with the the use of Qiangji Jianli method, further randomized clinical research are needed to clarify the exact mechanism of this phenomenon.

Keywords: Qiangji Jianli method, Neutrophil to lymphocyte ratio, Extended thymectomy, postoperative myasthenic crisis

P22: THE CLINICAL VALUE OF BIOMARKER IN THE THYMIC TUMORS

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Objective: This study was designed to evaluate the clinical significance of multiple tumor markers (CA-125, CEA, Cyfra, NSE and SCC) in the thymic tumors. **Methods:** Between the years of 2012 and 2014, the data of 313 patients who underwent thymectomy for thymic tumors in Shanghai Chest Hospital were retrospectively reviewed. The relations among tumor markers, pathological type, pathological stage and radical resection rate were analysed. **Results:** For the different pathological types of thymic tumors, the positive rates of CA-125 and Cyfra were significantly higher in the thymic carcinomas than the other types of thymic tumors (18.1% VS 6.2%, P<0.05 and 19.4% VS 2.9%, P<0.05). For the different stages of thymic tumors, the positive rates of CA-125 and Cyfra were significantly higher in stage III-IV disease than stage I-II disease (15.3% VS 6%, P<0.05 and 14.3% VS 3.3%, P<0.05). There was no significant difference in the positive rates of CEA, NSE and SCC for different pathological types and stage (P>0.05). No statistically significant difference of five biomarker positive rates was detected in the R0, R1 and R2 resections (P>0.05). Conclusions: CA-125 and Cyfra have certain clinical value in the diagnosis of thymic tumors. It is significant for predicting the pathological type and stage in the thymic tumors.

Keywords: thymic tumor, Tumor marker, stage, pathological type

P23: TUMOR VOLUME OF THYMIC EPITHELIAL TUMORS BASED ON WHO HISTOLOGICAL CLASSIFICATION

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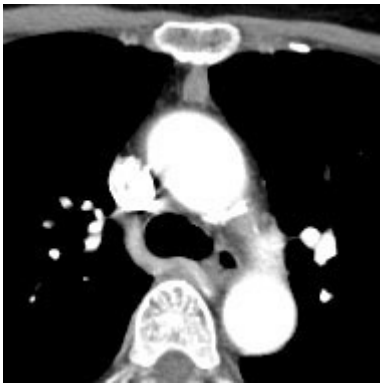
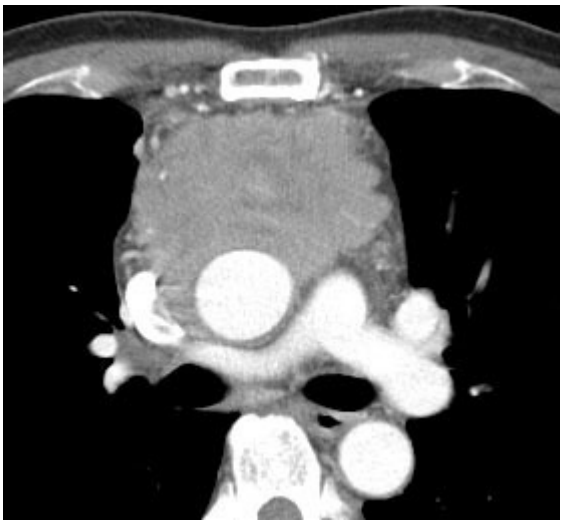
Purpose Our aim was to assess the tumor volume for various subtypes of thymic epithelial tumors based on the World Health Organization classification. **Methods** We retrospectively reviewed CT scans of 64 patients with thymic epithelial tumors pathologically proven by thymectomy or biopsy performed at our institution between January, 2010 and December, 2013. Forty-seven patients (two patients with type A, 13 with type AB, 14 with type B1, 12 with type B2, six with type B3), and 17 with thymic carcinomas were included. Tumor volumes were automatically calculated using a modified commercially available software [M.Y.1] (LISIT, Co., Ltd). We analyzed the correlation of the tumor volume and histological subtypes according to the World Health Organization classification using Mann-Whitney U test and Scheffe's F test. **Result** The measured tumor volumes ranged 0.502-46.9cm^3(mean ± SD: 64.9 ± 94.6). The tumor volumes(mean ± SD) in each WHO histologic type

were 127.1 ± 74.5 cm^3 in type A; 39.0 ± 35.1 cm^3 in type AB; 51.6 ± 104.6cm^3 in type B1; 45.1 ± 52.0cm^3 in type B2; and 29.5 ± 22.7 cm^3in type B3 tumors, respectively. The tumor volumes (mean ± SD) in thymic carcinoma were 114.7 ± 129.2 cm^3. There was no statistical significant difference in the volume of thymic epithelial tumors among each WHO histologic type or between low risk thymoma and high risk thymoma. (all comparison, P > .05) Significant advantages for differentiating tumors were observed between thymomas and thymic carcinomas in the tumor volume. Thymic carcinomas were significantly larger than thymomas. (P=.0080) **Conclusion** Thymic carcinoma tends to show larger tumor volumes than thymoma at the time of initial presentation. However, tumor volume may not be useful to differentiate among thymomas of each histological subtype.



thymoma type B1



thymic carcinoma

Keywords: WHO histological classification, tumor volume, thymic epithelial tumor

P24: THE PREDICTIVE ROLE OF THE WHO HISTOLOGICAL CLASSIFICATION IN THE TREATMENT OF ADVANCED THYMOMA

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Background and Objectives A recent report from the ITMIG has demonstrated that the WHO histological classification (WHO-HC) is not a prognostic factor for thymoma. We previously reported that the WHO-HC is a good predictive factor for therapeutic response in patients with advanced thymoma (Tagawa T et al. Surg Today 2011;41:1599-1604). The purpose of the present study is to examine the results of multimodal therapies for advanced thymoma and to reevaluate the predictive role of the WHO-HC using the updated data. **Patients and Methods** A retrospective review was performed on 54 patients with Masaoka stage III and IV thymoma who were treated from 1975 to 2014 at Kyushu University and the National Kyushu Cancer Center, Japan. The patient characteristics, treatment strategy, therapeutic response and outcomes were investigated in relation to the WHO-HC. **Results** Fifty-four patients (male, n=28; female n=26) underwent multimodal treatments at a median age of 58 years. The Masaoka stages of the patients were as follows: stage III (n=22; 41%), IVa (n=25; 46%) and IVb (n=7; 13%). Six patients had myasthenia gravis and 4 patients had pure red cell aplasia**.** As the initial therapy, surgery (S), chemotherapy (CT), radiotherapy (RT) and chemoradiotherapy (CRT) were performed in 25, 19, 5 and 5 patients, respectively. Macroscopic complete resection was achieved in 14 of 25 patients (56%). The 5-year and 10-year overall survival rates were 72.8% and 50.1%, respectively. An univariate analysis indicated that the WHO type A-B2 (p=0.029) and surgical cases (p<0.0001) were associated with a better prognosis. Of the 32 patients who did not undergo upfront surgery, or who underwent an R2 resection, 17, 8 and 7 patients were treated with chemotherapy, radiotherapy and chemoradiotherapy as the first-line treatment, respectively. The chemotherapy regimen included ADOC (cisplatin, doxorubicin, vincristine, cyclophosphamide) in 6 patients, cisplatin plus amrubicin in 5 patients, carboplatin plus paclitaxel in 2 patients, carboplatin plus etoposide in 2 patients and others in 9 patients. The response rate to the first-line therapy in the 19 patients with WHO type A-B2 was significantly better than that in the 13 patients with type B3, regardless of treatment modality (84.2% vs. 15.4%, p=0.0003, Table 1). Only the WHO-HC (A-B2 vs B3) was independently associated with the therapeutic response to first-line therapy (p<0.0001). **Conclusion** Type A-B2 thymoma showed a higher response rate to treatment than type B3. The WHO-HC is thus considered to be a good predictive factor for the therapeutic response in patients with advanced thymoma and should be used when determining the treatment strategy.

Table 1. Response to first-line therapy according to the WHO type and treatment modality

WHO type	Treatment modality						Total	
	Chemotherapy		Radiotherapy		Chemoradiotherapy			
	n	RR, %	n	RR, %	n	RR, %	n	RR, %
A - B2	11	82	3	100	5	80	19	84
B3	6	17	5	20	2	0	13	15
Total	17	59	8	50	7	57	32	56

RR: Response rate

Keywords: Thymoma, WHO histological classification, predictive factor

P25: VATS COMBINED WITH A SUBXIPHOID INCISION: A NOVEL APPROACH FOR LARGE THYMOMA

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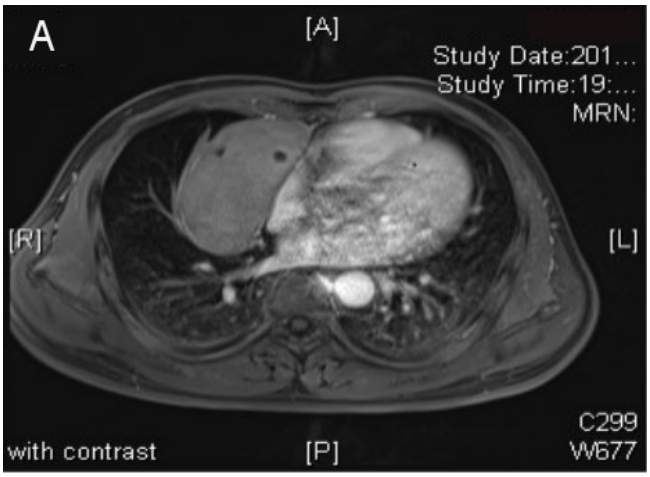
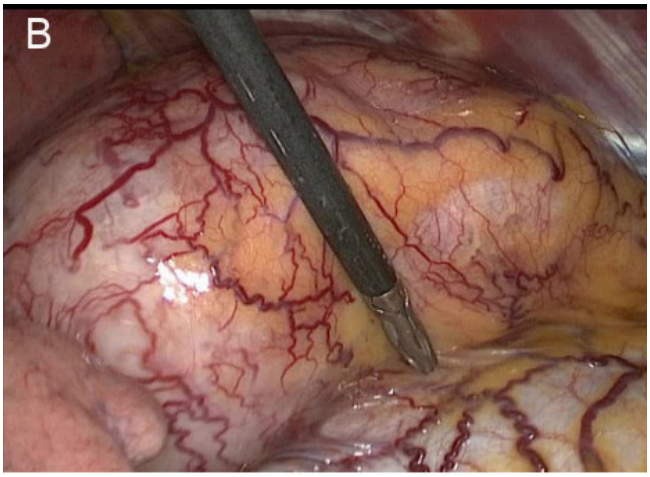
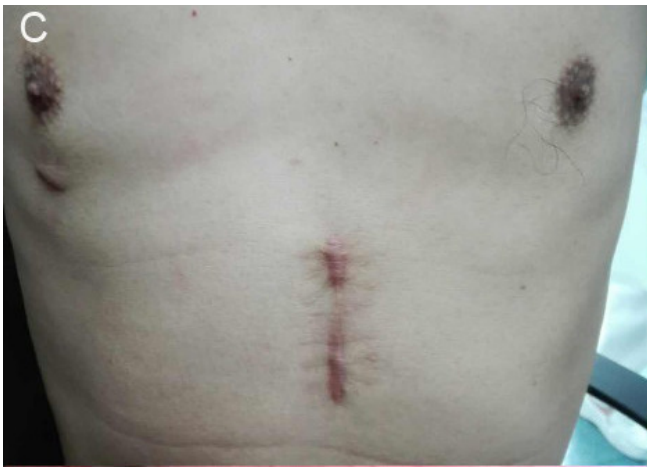
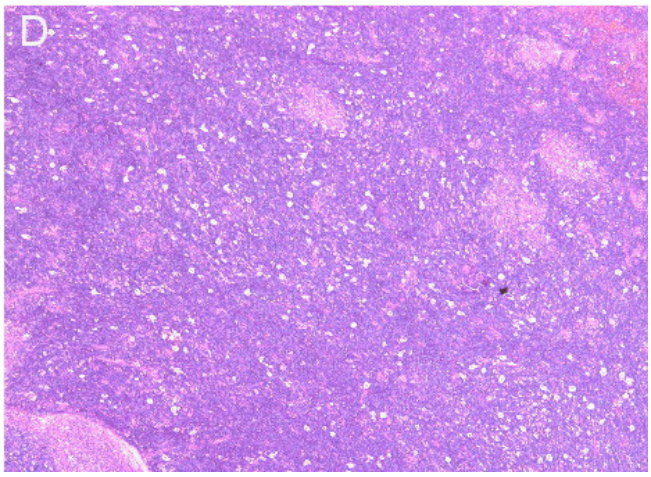
In patients with thymoma larger than 5cm in diameter, video-assisted thoracoscopic surgery (VATS) remains controversial as an approach for total thymectomy. Aside from the concerns such as possible rupture of tumor capsule, reduced safety margins and increased risk of local recurrence, how to remove specimen of this size from incisions of VATS is another problem that surgeons have to confront. We reported a case of a 47–year-old man who was referred to our department with a huge mass located on the anterior mediastinal and right hemithorax. After careful preoperative evaluation and planning, the tumor was completely removed by VATS and taken out of thoracic cavity through a subxiphoid incision.

After resection, histologic analysis confirmed the diagnosis of thymoma B1 type. Postoperative course was uneventful and no adjuvant therapy was offered. The patient has continued to do well with no signs of recurrence at a follow-up of 10 months. We stress that VATS combined with a subxiphoid incision may be a useful surgical option for patients with thymoma larger than 5cm in size. Fig 1. (A) Contrast MRI showed a huge anterior mediastinal mass occupying part of the right hemithorax. (B) Upon surgical exploration, the mass showed no adhesion to adjacent structures and was easily mobilized. (C) The subxiphoid incision after surgery. (D) Postoperative pathological examination indicated type B1 thymoma.









Keywords: Thymoma, Video-assisted Thoracoscopic Surgery, minimally invasive

P26: ANALYSIS OF IMMUNE MAKERS AND CLINICAL SIGNIFICANCE IN THYMOMAS WITH AUTOIMMUNE DISEASE IN THYMOMA

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Objective: To present the clinical experience in treating thymomas and thymomas with autoimmune disease (AD). To analyze the reason of the abnormal change of T iymphocyte subset and the correlation between thymoma and autoimmune disease **Methods:** The medical records of all 193 patients with thymoma in Tianjin Hospital from 2000 to 2015 were analyzed. According to that the patients with or without autoimmune disease were divided into two groups, T iymphocytes subsets were detected by fiow cytometry (FCM). The concentrations of serum IgG, IgM, IgA, C3, and C4 in individual patients were tested by enzyme-linked immunosorbent assay (ELISA). **Results:** The most frequent initial manifestations of thymoma were fatigable weakness of extraocula, bulbar and/or limb muscles (48.2%), followed by chest symptoms (22.8%) 13. 47%of the cases were accidentally found on routine chest roentgenogmphy. This group of patients had remarkable predisposition to autoimmunity, which was characterized by many kinds of autoantibodies detected among them. Thymomas is associated with a long list of autoimmune conditions (so-called paraneoplastic syndromes). The paraneoplastic syndmmes found in this group of patients included myasthenia gravis (48.2%), connective tissue diseases (4.16%), endocrinologic diseases (1.55%), hematologic disorders (2.07%), skin diseases (1.04%). The percentage of CD4+ cells and the ratio of CD4+/CD8+T cells was significantly increased in the AD group as compared with Tm, but there was no statistically significant difference in the percentage of CD8+T ceils between the two groups, Furthermore, there was no significant difference in the levels of serum IgG, IgA, IgM, and C4 among these groups of patients (P>0.05). In contrast, the concentrations of serum C3 in the Tm group were significantly higher than that in the MG and AD groups of patients (P<0.05), while INF-r,IL-4,C3 were significantly lower (P<0.05). **Conclusions:** The climcal manifestations of thymoma are variable. Patients with thymoma show significant predisposition to autoimmunity and thymomas is associated with many autoimmune disorders. There is an abnormal distribution of T cell subsets and level of cytokines and immune globulin in AD patients. Testing expression of immune makers will be helpful for predicting the clinical diagnosis and prognosis of thymoma with autoimmune disease.

Keywords: Thymoma, autoimmune disease, clinical significance, immune makers

P27: INDUCTION BUT NOT EXTRAPLEURAL PNEUMONECTOMY MAY BE IMPORTANT IN THE TREATMENT FOR STAGE IVA THYMOMA

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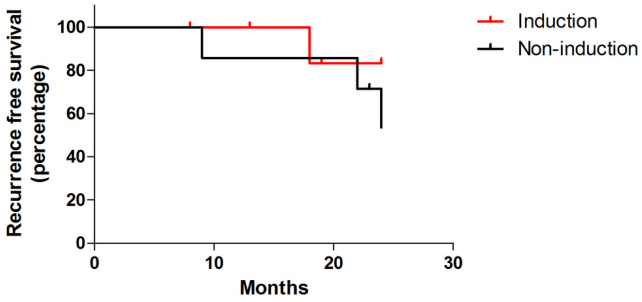
Aims: To retrospectively evaluate the results of surgical resection, including extrapleural pneumonectomy and local resection of pleural implants, in combination with adjuvant radiotherapy with or without induction therapy for the treatment of Masaoka stage IVa thymoma in our institution. **Methods:** From October 2008 to October 2014, 15 consecutive patients with stage IVa thymoma underwent radical resection followed by adjuvant radiotherapy. Eight patients had neoadjuvant chemo or chemoradiotherapy and the rest had no induction. Extrapleural pneumonectomy (EPP) was performed on one patient in the induction group and two in the non-induction group. The other patients had extended thymectomy plus local resection (LR) of invaded organs and pleural/pericardial implants. Median follow-up duration was 23 months (interquartile range, 18-30 months). Perioperative results and recurrence free survival were analyzed. **Results:** Overall mortality and in-hospital morbidity were 0 and 33.3% respectively. In the induction group, the response rate was 50% (3 partial responses and 1 complete pathological response). In-hospital morbidity was insignificantly more favorable in the induction group (12.5% vs 57.1%, p = 0.10, Fisher's test) especially in the responsive patients (0/4). EPP was associated with increased hemorrhagic events (100% vs 8.3%, p < 0.01, Fisher's test) and prolonged length of ICU stay (median 7 vs 3 days, p = 0.02, Mann Whitney test). Overall 1- and 2-years recurrence rates were 6.7% and 26.7% respectively and patients after induction had lower recurrences at 2 years (12.5% vs 42.9% in the non-induction group). Notably, none of the induction responsive patients but two of the EPP patients had their diseases relapsed during the follow-up time. **Conclusions:** Neoadjuvant chemotherapy seems to be a beneficial addition to surgery and adjuvant radiotherapy for stage IVa thymoma. EPP is a more traumatic procedure and whether it may bring any survival advantage is still debatable.



Keywords: Extrapleural pneumonectomy, Induction, Stage IVa thymoma

P28: PRIDICTORS AND MANAGEMENT FOR THE PRIMARY IVA THYMOMA

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Purpose: We aimed to evaluate the multimodality treatment of prognostic for the patients with IVa thymoma. **Materials and Methods:** We enrolled 50 consecutive patients with primary IVa thymoma (WHO) treated in the Chest Hospital, China from Jan 2006 to December 2013. The median age was 45 years (25–70 years). The distribution of WHO pathological type was B1 3(6%), B2 14(28%), B3 25(50%), B thymoma but indetermination 8(16%), respectively. The media maximum diameter of the primary tumor and pleural tumor were 8.5 centimetre (3-22cm) and 2.2cm (0.5-5cm). For the initial treatment, 32 (64%) patients underwent extended surgery. 22 patients received chemotherapy and 35 patients received subsequent mediastinal radiotherapy (MRT) or plural radiotherapy (PRT). **Results:** The median follow-up interval from the initial diagnosis was 37 months (range, 12–94 months). Five-year survival was 51%. Pleura was the most common site of recurrence and progress (14 patients in the surgery group,45%). There were significant differences for five-year-survival between the patients with or without surgery (62.6% for surgery Vs. 35.6% for no-surgery patients, p = 0.011) .and between the patients with or without radiotherapy (60.7% for RT Vs. 33% for no-RT patients, p = 0.00) In univariate analysis, the complete resection of the primary mediastinum tumor, the resection of the plural tumor, surgical management and PRT showed an good effect of on OS. In multivariate analysis, only plural radiation was associated with prolonged survival (p=0.041). For the surgery group, the plural metastasis number more than four on the CT before surgery was significant risk factors for recurrence, while the non-complete resection of the primary mediastinum tumor was significant risk factors for overall survival . For the non-surgery group, radiation (include MRT and PRT) was the only independent factors predicting long-term survival. Chemotherapy was associated neither with improved progression-free survival for the non-surgery group (p=0.771) nor with freedom-from-recurrence for the surgery group. **Conclusion:** For the patients of primary Iva stage thymoma, our retrospective analysis showed that complete resection of the primary mediastinum tumor and PRT were associated with better outcome. Nevertheless, there were adjuvant PRT after surgery and PRT aimed at the recurrent plural when recurrence in our date. We have no idea when and how PRT take part in the treatment progress. Further prospective studies are warranted to clarify the role of RT in the treatment of these patients.

P29: EVOLUTION OF MINIMALLY INVASIVE SURGERY IN THE MANAGEMENT OF THYMIC MASSES AT A SINGLE INSTITUTION

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Introduction: Thymic masses may result due to benign or malignant processes. The optimal surgical approach in the management of these masses remains controversial. The aim of this study was to review our experience in surgical resection of thymic masses, and present outcomes from various surgical approaches. **Methods:** A retrospective review was conducted on patients with surgically resected thymic masses from 2000 to 2014 at our institution. Data collected included: patients' demographics, clinical presentation, myasthenia gravis, medical co-morbidities, radiological findings, histological types and stages. Surgical approaches and post-operative outcomes were also analyzed. Outcomes were stratified according to the main surgical approaches: Open, Video-assisted Thoracoscopic Surgery (VATS) and Robotic-assisted Thoracic Surgery (RATS). **Results:** Seventy-one patients were eligible for this study. Median age was 48 years (range 18-78) and 37 were female. Forty three patients had a diagnosis of myasthenia gravis and 17 patients received intra-venous immunoglobulin (IVIG) treatment pre-operatively. Other common medical co-morbidities were hypertension (n=22), hyperlipidaemia (n=19) and diabetes (n=9). Twenty patients underwent open surgery via median sternotomy (MS), 22 underwent VATS, and 29 had RATS. Median operative time was 100 minutes for both open and robotic surgery, and 143 minutes for VATS. There were 3 conversions from VATS to open surgery, but none for RATS. Post-operative complications occurred in 4 MS and 3 VATS patients. There was no mortality. Median length of stay was 5 days for open surgery, 4 days for VATS and 2 days for RATS. Thymomas were the most common histological diagnosis (n=34).

Table 1: Classification of Myasthenia Gravis and Thymoma Histopathology

Characteristic	Open (n=20)	VATS (n=22)	Robot (n=29)	Total
Myasthenia Gravis	11	17	15	43
MGFA class 1	4	3	7	14
MGFA class 2	5	12	8	25
MGFA class 3	1	1	0	2
MGFA class 4	1	0	0	1
MGFA class 5	0	1	0	1
Thymoma	13	9	12	34
Masaoka Stage 1	5	1	4	10
Masaoka Stage 2	2	4	5	11
Masaoka Stage 3	0	3	2	5
Masaoka Stage 4a/b	6	1	1	8
WHO Grade A	4	0	0	4
WHO Grade AB	2	2	2	6
WHO Grade B1	2	0	3	5
WHO Grade B2	2	4	3	9
WHO Grade B3	1	3	2	6
WHO Grade C	1	0	1	3

Conclusion: Our study demonstrates that minimally invasive approaches (VATS and RATS) for thymic masses are safe and associated with low morbidity and mortality. RATS is now the approach of choice at our Institution.

Keywords: Robotic surgery, Video-assisted Thoracoscopic Surgery (VATS), Robotic assisted Thoracic Surgery (RATS), Thymoma, Thymic mass

P30: A CASE OF ANTERIOR MEDIASTINITIS AND BILATERAL MULTIPLE LUNG ABSCESSES OCCURRING AFTER TSTET

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Trans-subxiphoid thoracoscopic extended thymectomy (TsTET), which can provide a better exposure of bilateral upper thymus lobes and the contralateral phrenic nerve, was reported superior to unilateral thoracoscopic approach in treatment of myasthynia gravis or anterior mediastinal tumour. However, the postoperative complications for TsTET have hardly been discussed. Here we reported a 68-year-old female suffered subxiphoid incision infection, anterior mediastinitis, concomitant bilateral pneumonia and multiple lung abscesses after TsTET. In our experience, because the subxipoid incision, the anterior mediastinum and the bilateral thoracic cavity communicated directly after TsTET, it should be aware of the risk of infection in anterior mediastinitis and bilateral thoracic cavity following subxiphoid incision infection.

Keywords: myasthenia gravis, mediastinitis, thymectomy

P31: SALVAGE SURGERY FOR PMGCT: BENEFICIAL FOR PERSISTENT POSITIVE-MARKER PATIENTS?

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Background: Primary mediastinal germ cell tumors (PMGCT) are rare and high-grade malignant tumors. Mainstay treatment for PMGCT is systemic chemotherapy, and salvage surgery for residual tumor is considered in patients with normalized tumor makers. However, survival benefit of salvage surgery for persistent positive-marker patients remains unclear. Purpose: To clarify the outcome of salvage surgery for PMGCT. **Methods:** A total of 8 patients undergoing salvage surgery for PMGCT in our institution from July 2000 to February 2013 were enrolled. Surgical outcomes of these patients were retrospectively analyzed. **Results:** All patients were men and the median age was 25 years (range, 18-37). Histological type was seminoma in 1 and non-seminomatous germ cell tumor in 7. Serum alpha-fetoprotein (AFP) level was initially elevated in 7 patients. All patients received primary chemotherapy consisting of bleomycin, etoposide, and cisplatin with a median cycle of 3 (range, 3-4). Four patients additionally received 2nd (n=2), 3rd (n=1), or 4th (n=1) line chemotherapy. AFP level normalized in 5 patients. Complete R0 resection was achieved and serum AFP level normalized in all patients. Median duration of postoperative hospital stay was 7 days (range, 5-11), and there was no morbidity or mortality. Pathological complete response was observed in 4 patients. The median recurrence-free and overall survival (RFS and OS) periods for all 8 patients were 31 (range, 6-74) and 31 (range, 15-74) months, respectively. All of the 5 patients with preoperatively normalized AFP levels were alive without recurrence, with a median follow-up period of 56 (range, 26-74) months. Of the 3 persistent AFP-positive patients, 2 were alive without recurrence at 24 and 33 months after surgery. **Conclusion:** We confirmed that complete resection of residual PMGCT achieved favorable prognosis in patients with preoperatively normalized AFP levels. This study suggests that salvage surgery might be beneficial even in persistent positive-marker patients if complete resection is deemed possible.

Keywords: Primary mediastinal germ cell tumors (PMGCT), salvage surgery, AFP, complete resection

P32: COMPARING RADIOTHERAPY WITH FREE BREATHING AND DEEP INSPIRATION BREATH HOLD FOR THYMIC CANCERS

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Background: Patients with thymic epithelial tumours (TET) have an excellent prognosis. Radiotherapy (RT) is used in the treatment of thymomas as adjuvant treatment after surgery or, if surgery is not possible, as the primary local treatment. High doses of radiation delivered to normal tissue may result in increased morbidity and mortality. We investigated whether RT with deep inspiration breath hold (DIBH) reduces the radiation dose to normal tissues compared to RT in free breathing (FB). **Patients and Methods:** Seventeen patients with TETs and a treatment planning scan done both with FB and DIBH is included in the study. Treatment plans will be calculated in both FB and DIBH. We will estimate the mean dose to the heart, and lung, and the relative volumes of heart, and lung receiving 20 and 30 GY. The differences in these dose characteristics are tested with Wilcoxon signed-rank test. **Results:** We have identified 17 patients with TETs who have been treated with RT in doses of at least 50 gy and who had a therapy planning CT scan with both FB and DIBH. Five patients were treated with curative intent and 12 in the adjuvant setting. All patients were treated in 2 gy fractions. Ten patients received doses of 50-54 gy and 7 patients received 60-66 gy. The mean doses to the heart and lung are estimated as well as the relative volumes of heart, and lung receiving 20 and 30 GY. A full dataset will be presented at the meeting.

Keywords: Radiation Therapy, Deep inspiration breath hold, Redio-therapy

P33: PREDICTIVE FACTORS OF EXTENDED THYMECTOMY FOR MYASTHENIA GRAVIS

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Background: Extended thymectomy as a treatment strategy in myasthenia gravis (MG) is supported by some reports. Improvement in myasthenic symptoms after extended thymectomy occurs in 60% of patients, but improvement factors of extended thymectomy for MG remain controversial. **Methods:** We reviewed the clinical

outcomes of 28 patients (11 males, 17 females; median age 57 years) who underwent extended thymectomy for MG at our hospital between 2005 and 2014. We analyzed the following factors influencing outcome: age, gender, Myasthenia Gravis Foundation of America (MGFA) Clinical Classification, serum level of anti-acethylcholine receptor antibody, presence of thymoma, medication requirements before and after extended thymectomy, and duration from onset to surgery. **Results:** There was complete remission in 3 patients (10.7%), palliation in 17 patients (60.7%), no change in 5 patients (17.9%), deterioration in 3 patients (10.7%), and death in 2 patients (7.1%). The preoperative MGFA Clinical Classifications were I, IIa, IIb, IIIa, and V in 4, 17, 1, 3, and 3 patients, respectively. There were 13 nonthymomatous patients and 15 thymomatous patients. Preoperative median serum level of anti-acethylcholine receptor antibody was 20nmol/ml, and 24 patients received preoperative steroid administration (85.7%). Patients receiving preoperative steroid administration showed significant postoperative improvement in myasthenic symptoms (p=0.035). There was a tendency for improved myasthenic symptoms in males and patients with MGFA Clinical Classification IIa (p=0.052 and p=0.078, respectively). Age of the patient, serum level of anti-acethylcholine receptor antibody, presence or absence of thymoma, and duration from onset to surgery were not found to be significant prognostic factors. **Conclusions:** The present study showed that extended thymectomy with preoperative steroid administration is an effective therapy for myasthenia gravis. Further studies based on a larger series are needed to confirm these preliminary data.

Keywords: steroid, Extended thymectomy, myasthenia gravis, Predictive factors

P34: THE CLINICAL ANALYSIS OF SUBXIPHOID APPROACH OF VATS ANTERIOR MEDIASTINAL MASS EXTENDED RESECTION

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Objective: To evaluate the feasibility and effectiveness of the subxiphoid approach of video-assisted thoracoscopic anterior mediastinal mass extended resection. **Methods:** Between December 2014 and June 2015, 11 patients with anterior Mediastinal mass were enrolled in this study.5 cases were male and 6 cases were female. The average age was 47 (23-69). They all underwent subxiphoid video-assisted thoracoscopic extended thymectomy (SxVATET). As those with myasthenla gravis, the bilateral mediastinal fatty tissue was resected. The operation time, tumor size, blood loss and thoracic drainage period were recorded. **Results:** The postoperative pathologies including thymic hyperplasia in 2 cases, thymoma in 3, thymic cyst in 2, bronchial cyst in 3, and mesothelium cyst in 1. The mean operation time, size of tumor, blood loss and thoracic drainage period were 90 (60–120) min, 3. 1 (1. 5~ 5.3)cm, 27 (10~100) ml, and 1.9 (1–3) days, There were no surgical complications or mortalities, and the cosmesis is satisfying. **Conclusions:** Our experience demonstrates that SxVATET provides an excellent view of the bilateral pleural cavities. Resecting ample bilateral mediastinal fatty tissue in addition to the thymic gland, can be safely undertaken. Besides, the procedure is minimal invasive with a few postoperative complications and good cosmetic outcomes. But long-term outcomes still need further research.

Keywords: thymectomy, subxiphoid approach, video-assisted thoracoscopic

P35: STUDY ON THE LOSS OF HETEROZYGOSITY OF MICROSATELLITE ALLELE IN THYMIC EPITHELIAL TUMORS

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Objective: To study the relationship between loss of heterozygosity (LOH) on Human Leukocyte Antigen (HLA) locus and the pathogenesy and clinicopathological features of thymic epithelial tumor. **Methods:** Choose 36 thymic epithelial tumor patients in Tianjin Medical University general hospital. Amplify 5 microsatellite locus (D6S1666, D6S265, D6S273,DS6276 and D6S291) of 36 thymic epithelial tumors and paired normal tissues by PCR. Detect the condition of base loss using DNA sequencing technique. Analyze the frequency of microsatellite LOH. **Results:** 83.6% of the thymic epithelial tumors showed LOH on at least one locus; The rate of LOH which was detected at loci of D6S1666,D6S265,D6S273,D6S276 and D6S291 was 44.4%, 16.7%, 30.5%, 38.9% and 36.1% separately. There is no significant association between LOH with thymic epithelial tumor with or without myasthenia gravis (MG) and the benign or malignant thymic epithelial tumor. **Conclusions:** D6S1666, D6S265, D6S273, DS6S276 and D6S29 are sensitive loci for studying microsatellite DNA in thymic epithelial tumor. LOH on HLA complex play a certain role in occurrence and development of thymic epithelial tumor, the most likely involving gene is HLA-DQA1, but the relationship between LOH and clinicopathological features of thymic epithelial tumor needs to expand the sample size for further study.

Keywords: thymic epithelial tumors, microsatellite allele, LOH, HLA

P36: THORACOSCOPIC RESECTION OF BULKY THYMOMA USING ARTIFICIAL PNEUMOTHORAX

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Objective To explore the feasibility and efficacy of thoracoscopic radical resection of huge retrosternal thymoma using artificial pneumothorax. **Methods** A retrospective analysis was performed on 19 patients with bulky thymoma who underwent thoracoscopic resection using artificial pneumothorax by CO2 insufflation. **Results** The operations were performed with unilateral or bilateral thoracic incisions via single lumen endotracheal intubation and two-lung ventilation. And this approach provided excellent exposure of the thoracic cavity and reliable control of the neuro-vascular structures in the anterior mediastinum, which was of vital importance for extended resection of malignant thymoma. Besides, the operation time was (140.0±51.4) min without conversion to thoracotomy or sternotomy. And the pathological diagnosis was confirmed by immunohistochemistry, including 5 cases of thymus lipomyoma, 1 case of thymus hyperplasia, 1 case of thymus cyst, 2 cases of type AB thymoma, 4 cases of type B1 thymoma, 4 cases of type B3 thymoma, and 2 cases of thymic carcinoma. Furthermore, there were no complications such as recurrent laryngeal nerve injury, phrenic nerve injury, pulmonary infection or atelectasis, with hospital stay of (5.0±3.0) d. **Conclusion** Thoracoscopic resection of thymoma using artificial pneumothorax is a preferable approach, which could be considered for patients with bulky retrosternal tumors.

Keywords: Artificial pneumothorax, Two-lung ventilation, Thymoma

P37: LOCALLY ADVANCED THYMOMA - ROBOTIC APPROACH

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Objective: The conventional approach to locally advanced thymoma has been via a sternotomy. VATS and robotic thymectomies have been described but typically are reserved for patients with myasthenia gravis only or for small, encapsulated thymic tumors. There have been few reports of minimally invasive resection of locally advanced thymomas. Our objective is to present a case in which a large, locally advanced thymoma was resected en bloc with the pericardium employing robotic assisted thoracoscopic approach. Case Summary: This case illustrates a case of an asymptomatic 29 year old female found to have an 11 cm anterior mediastinal mass on CT scan. A right-sided, 4 port robotic approach was utilized with the camera port in the 5th intercostal space anterior axillary line and two accessory ports for robotic arm 1 and 2 in the 3rd intercostal space anterior axillary line and 8th intercostal space anterior axillary line. A 5 mm port was used between the camera and 2nd robotic arm for assistance. On exploration the mass was found to be adherent to the pericardium that was resected en bloc via anterior pericardiectomy. Her post-operative course was uncomplicated, and she was discharged home on postoperative day one. Final pathology revealed an 11x7.5x3.0cm WHO Class B2 thymoma invading the pericardium, TNM stage T3N0M0, with negative margins. The patient was subsequently sent to receive 5,040 cGy of adjuvant radiation, and follow-up CT scan 6 months postoperatively showed no evidence of disease. **Conclusion:** Very little data exist demonstrating the efficacy of resecting locally advanced thymomas utilising the minimally invasive approach. Our case demonstrates that a robotic assisted thoracoscopic approach is feasible for performing thymectomy for locally advanced thymomas. This may help limit the morbidity of a trans-sternal approach while achieving comparable oncologic results. However, further studies are needed to evaluate its efficacy and long term outcomes.

Keywords: Robotic Thymectomy, Thoracoscopic Thymectomy, Locally Advanced Thymoma, Thymoma

P38: REOPERATION FOR RECURRENT THYMOMA: A SINGLE-CENTER EXPERIENCE FROM NANCHANG

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Objective: To analyze causes for recurrence of thymoma after primary operation, explore the relation between thymoma and myasthenia gravis, and summarize surgical treatments for recurrent thymoma. **Methods:** 5 cases of recurrent thymoma were re-operated. At primary operation all patients were complicated with myasthenia gravis, including one type I, one type IIa, one type IIb and two type C thymoma according to Osserman classification. Upon reoperation, none of these patients manifested with myasthenia gravis; and pyridostigmine bromide was withdrawn after one to six years since symptoms of myasthenia gravis were totally relieved. Post-operatively histological diagnosis were made according to the WHO classification (primary operation: three type B2 case, one type B3 case and one type C case; reoperation: three type B2 case and two type C case) and the Mashaoka system (three IIb case and two III case in both primary operations and reoperations). Among these recurrent cases, one case recurred diffusively in the left pleura, left lung and left ribs, with one positive lymph node(1/10); one case recurred in the right chest cavity and transferred to the left inferior lobe; one case recurred in the right chest cavity and the right inferior lobe; one case recurred in the mediastinum, left upper lobe and the pericardium; yet another case recurred in the mediastinum, the right chest cavity, right upper lobe, superior vena cava and brachiocephalic vein. Reoperation was carried out in all recurrent cases. Sternotomy was performed in one patient for resection of mediastinal tumor, pneumonectomy and replacement of brachiocephalic vein and superior vena cava with artificial blood vessel. Video-assisted thoracic surgery(VATS) was performed in two cases, namely, resection of mediastinal tumor, part of left upper lobe, pericardium and the left phrenic nerve and resection of part of right lower lobe and tumor in the right thoracic cavity. Left posterolateral thoracotomy for resection of part of left upper lobe, pleural tumor and invaded ribs was performed in one patient. Yet one patient was procedured for left lower lobectomy through posterolateral thoracotomy and resection of the recurrent thymoma via VATS in the right thorax. **Results:** One patient died of respiratory failure in the 14th postoperative day. Two patients died of multi-organ dysfunction in the 25th and 36th postoperative month, respectively. Two patients survived and pyridostigmine bromide was withdrawn after the symptoms of myasthenia gravis were totally relieved one to six years post-operatively. **Conclusions:** 1.We proposed that thymoma recurs mainly in forms of recurrence in situ and seeding in the chest cavity, instead of metastasis via lymphatic pathway. 2. Recurrence of thymoma is highly related to histological types and pathological characteristics. 3. Symptoms of myasthenia gravis in recurrent patients are not highly related to the severity of the recurrent thymoma. 4. Reoperation must be performed thoroughly without tissue fragments reserved, thoracic irrigation in the end of procedure can help elimination of those fragments. Chemotherapy should be implemented in patients diagnosed with thymoma of pathological type B2 and C. Regular CT scan can help early diagnosis of recurrence, which should be reoperated without delay.

Keywords: Thymoma, recurrence, reoperation

P39: EFFECTS OF TNIP1/TNFAIP3 EXPRESSION: IMPLICATIONS FOR MYASTHENIA GRAVIS

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Objective NF-κB pathway participates in the process of a variety of auto-immune diseases, TNIP1 and TNFAIP3 are crucial negative-regulating factors for this pathways. The aim of this study is to figure out whether TNIP1/TNFAIP3 plays a positive role on the occurrence of myasthenia gravis (MG). **Method** Real-time PCR was applied to quantify the expression level of TNIP1 and TNFAIP3 in thymocytes from 11 MG patients and 12 heart surgery cases. The difference of TNIP1 expression of MG thymocytes and normal thymocytes was evaluated. Similarly, the comparison of these two cohorts for TNFAIP3 expression was conducted. Result TNIP1 expression in MG thymocytes was lower than normal thymocytes significantly. However, no difference was detected when it came to the analysis of TNFAIP3. **Conclusion** Decrease of TNIP1 expression devotes to the occurrence of myasthenia gravis possibly.

Keywords: myasthenia gravis, TNIP1, TNFAIP3

P40: DOES IL8 (CXCL8) HAVE A ROLE IN THYMOMA PROGRESSION AND AS A MARKER FOR RELAPSE?

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Thymomas are rare tumours of thymic epithelium for which surgical resection is the definitive treatment. The thymus is the organ in which T cells mature. During development in the thymus, T cells acquire their unique T cell receptor (TCR) through somatic recombination. Mature naïve T cells that exit the thymus harbour small circles

of DNA that are by-products of somatic recombination known as T cell receptor excision circles (TRECs). Although stable, TRECs are not replicative and hence are a marker of recent thymic emigrants (RTEs). We have recently shown that thymocytes and subsequently RTEs, unlike more mature peripheral blood T cells, produce the cytokine interleukin 8 (IL8/CXCL8). This ability appears to be lost with repeated stimulation and expansion. Therefore, T cell production of IL8, like TREC levels, is a marker of RTEs and thymic activity. Our recent data proposes two questions in relation to this tumour type 1. Could IL8 together with TREC levels act as a biomarker for tumour recurrence? 2. Does IL8 have a role as a growth factor for thymoma? After resection, macroscopic recurrence is usually detected in patients by active surveillance with serial axial imaging. There is some data in the literature to suggest that TREC levels are higher in patients with recurrence compared to those without. This raises the possibility of using RTEs to aid in surveillance and guide the judicious use of imaging. Our initial data suggests that even after R0 margins, both TRECs and IL8 producing T cells can be detected in the periphery, albeit at very low levels. However, we hypothesize that intra-patient monitoring of TREC levels and IL8 producing T cells may still be useful as a biomarker for recurrence. Moreover, the fact that IL-8 is associated with tumour maintenance through its functions in angiogenesis; cancer cell growth and survival; and modification of immune responses, indicates that this may be an important growth factor in thymoma. We hope to address this using resected material in comparison with normal thymuses.

Keywords: Biomarker, TREC, RTE, IL8

AUTHOR INDEX

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