Kazuhiko Koike

I am Kazuhiko Koike, President of the Organization of Japan Digestive Disease Week (JDDW). It is a great pleasure for me to announce and host the 7th JDDW-KDDW-TDDW (JKT) joint symposium in Kobe. Through the past six occasions, various improvements have been made by the efforts of the respective DDWs, which have indeed fostered this academic activity to become more and more mature and meaningful. This 7th JKT joint symposium will be held as parallel sessions using two rooms in order to secure enough time for deeper discussions on the respective important topics of the upper GI, lower GI liver and pancreato-biliary categories. In addition, proceedings of the joint symposium will be prepared so that the JKT joint symposium will become a precious opportunity to promote collaborations for clinical research work among investigators of the 3 DDWs.

At the beginning of 2023, the 8th wave of COVID-19 caused by the SARS-CoV Omicron strain is finally coming to an end in Japan, and Japan government has executed the plan of the class change of SARS-CoV infectious diseases from category 2 to 5. Although there are still some uncertainties, I hope that many of you will visit Kobe, and that it will be a fruitful academic meeting.

Finally, I would like to express my heartfelt appreciation to the executive board members of the KDDW and TDDW, and all the presenters, moderators and discussants of this symposium for your kind understanding and warm support.

President, Japan Digestive Disease Week

Jae Gyu Kim

I would like to congratulate JDDW 2023 and the 7th Joint Session between JDDW-KDDW-TDDW 2023 as the representative of Korean Digestive Disease Week 2023 and the Korean Society of Gastroenterology. I am really grateful to the JDDW 2023 Steering Committee for preparing well even under difficult circumstances. The Joint Session between JDDW-KDDW-TDDW 2023 has developed by the continuous efforts from JDDW of Japan, KDDW of Korea and TDDW of Taiwan until now. I think our three countries have to develop the Joint Session even more based on these good collaboration and foundation so far. I am very pleased to see that these goals are gradually being realized after I look through the contents of the program. I am confident that our researchers and scholars from three countries will be able to enjoy a festival where they share new knowledge and interests in the field of gastroenterology. In addition, I would like to say that our three countries need to work together for further development based on this Joint Session. The 8th Joint Session will be held in Korea next year. We will do our best to make it a great success. Lastly, I would like to express my deepest gratitude to everyone who prepared for the Joint Session between JDDW-KDDW-TDDW 2023 and to those who attended.

President, Korea Digestive Disease Week 2023
President, The Korean Society of Gastroenterology

Ming-Shiang Wu

Dear Esteemed Colleagues and Distinguished Guests,

On behalf of the Gastroenterological Society of Taiwan (GEST), it is my great pleasure to extend a warm welcome to the first in-person meeting of the Japan-Korea-Taiwan (JKT) joint session at JDDW 2023. This significant event marks a momentous occasion as we convene for the first time in person after enduring the challenges posed by the COVID-19 pandemic. The resilience and commitment of our medical communities have allowed us to come together again, fostering the spirit of collaboration and knowledge exchange. Japan, Korea, and Taiwan share not only common digestive disease patterns but also similar trajectories in economic development and healthcare systems. These similarities create a unique synergy that enhances our collective ability to address the complexities of digestive health. This joint session stands as an ideal platform for clinicians and researchers from these three countries to share cutting-edge knowledge and the latest advances in digestive medicine.

In this collaborative environment, I am confident that our shared expertise will pave the way for innovative breakthroughs, ultimately benefiting patients across our nations. I encourage all participants to actively engage in discussions, foster partnerships, and explore new avenues of research. I extend my heartfelt gratitude to everyone involved in organizing this event, and I eagerly anticipate fruitful discussions, inspiring insights, and lasting collaborations.

Thank you for your dedication to advancing the field of gastroenterology. Together, let us embark on this journey of knowledge exchange and transformative progress.

Warm regards,

Prof. Ming-Shiang Wu
President, The Gastroenterological Society of Taiwan (GEST)
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Abstract
**Lower GI**

**Recent updates in multidisciplinary treatment for colorectal cancer in Asia**

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Department of Surgical Oncology, The University of Tokyo Graduate School of Medicine, Japan

Chair (K): Tae Il Kim  
Department of Internal Medicine, Yonsei University College of Medicine, Korea

Chair (T): Han-Mo Chiu  
National Taiwan University Hospital, Taiwan

Discusser (J): Yosuke Fukunaga  
Department of Gastroenterological Surgery, Gastroenterological Center, Cancer Institute Hospital, Japan

Discusser (K): Bo-In Lee  
Department of Internal Medicine, The Catholic University of Korea College of Medicine, Korea

Discusser (T): Chien-Chih Chen  
Koo Foundation Sun Yat-Sen Cancer Center, Taiwan

Speaker (J):  
**JKT1-1**  
Evolution of lower rectal cancer treatment with multidisciplinary approach.  
Yuji Toiyama  
Department of Gastrointestinal and Pediatric Surgery, Division of Reparative Medicine, Institute of Life Sciences, Mie University Graduate School of Medicine, Tsu, Japan

Speaker (K):  
**JKT1-2**  
Long-term Outcomes of Endoscopic Resection in T1 Colorectal Cancer and Strategies for Determining Additional Surgery  
Yunho Jung  
Department of Internal Medicine, Soonchunhyang University College of Medicine, Cheonan, South Korea

Speaker (T):  
**JKT1-3**  
Adding bevacizumab to neoadjuvant chemoradiotherapy increases pathological complete remission and survival in patients with locally advanced rectal cancer  
Jason Chia-Hsien Cheng  
Department of Oncology, National Taiwan University Hospital, Taiwan

Rising Star Program (J):  
**JKT1-RS1**  
Colonoscopy for colorectal cancer screening and management of early colorectal cancer  
Masau Sekiguchi  
Cancer Screening Center/Endoscopy Division, National Cancer Center Hospital, Tokyo, Japan

Rising Star Program (K):  
**JKT1-RS2**  
Recent advances in multidisciplinary treatment for colorectal cancer  
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Rising Star Program (T):  
**JKT1-RS3**  
Role of endoscopic muscular dissection for rectal cancer with clinical complete response after concurrent chemoradiotherapy  
Chao-Wen Hsu  
Division of Colorectal Surgery, Kaohsiung Veterans General Hospital, Taiwan
Evolution of lower rectal cancer treatment with multidisciplinary approach.

Yuji Toiyama¹), Mikio Kawamura¹), Yoshinaga Okugawa²)

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In Japan, historically, surgery is the primary treatment for lower rectal cancer. Total mesorectal excision (TME) has established the standard surgical approach for rectal cancer since 1980 and has significantly improved local control and survival rates. In addition, from evidence achieved by JCOG0212, the JSCOR Guidelines recommend performing TME with lateral lymph node dissection (LLND) for cT3 or deeper lower rectal cancer.

In the West, the therapeutic effects of extended lymph node dissection including with LLND were reported in the 1950s. However, due to a high incidence of distant recurrence and postoperative sexual and urinary dysfunction, several clinical trials demonstrated the usefulness of radiation therapy with concurrent chemotherapy before surgery for the suppression of local recurrence. Since then, preoperative chemoradiotherapy (CRT) + TME has become the standard treatment.

Thus, while both preoperative CRT and LLND aim to control pelvic local recurrence, they face challenges in controlling distant metastasis and improving survival. In this context, a powerful preoperative treatment known as Total Neoadjuvant Therapy (TNT), which sequentially introduce radiation therapy and systemic chemotherapy before surgery, has been introduced in Western countries, and demonstrated further shrinking the primary tumor and reducing distant metastasis. The development of preoperative CRT for rectal cancer has resulted in an increase in cases achieving pathological complete response (CR). In 2004, Habr-Gama proposed the Watch & Wait approach, which involves avoiding immediate surgery and observing patients who achieve clinical CR after preoperative treatment. This approach has been validated as a safe and high-quality treatment primarily in Europe and the United States. It represents a significant shift from the conventional concept of surgery and is expected to increase the proportion of rectal cancer patients who can undergo organ preservation by introducing TNT in the preoperative treatment.

Advances in molecular profiling and genetic testing have enabled the identification of specific genetic mutations or biomarkers in rectal cancer. In particular, the patients with microsatellite satellite instability have merit to use immune checkpoint inhibitors, since high clinical CR rate in extremely high rate and non-operative management can be achieved. Overall, the evolution of lower rectal cancer treatment with a multidisciplinary approach has led to improved outcomes, reduced morbidity, and enhanced quality of life for patients.

Collaboration among surgeons, medical oncologists, radiation oncologists, pathologists, radiologists, and other healthcare professionals is crucial in delivering optimal care and tailoring treatments to individual patients.

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Curriculum Vitae

Yuji Toiyama
Department of Gastrointestinal and Pediatric Surgery, Division of Reparative Medicine, Institute of Life Sciences, Mie University Graduate School of Medicine, Tsu, Japan

Name: Yuji Toiyama, MD, PhD, FACS
Date of Birth: July 25, 1969
Present Academic Rank and Position: Professor of both Department of Gastrointestinal & Pediatric Surgery and Innovative Surgery and Surgical Techniques Development, Division of Clinical Sciences, Mie University Graduate School of Medicine in Japan.
Research Career and Experience:

1. Education:
1997: MD, Mie University School of Medicine
2005: Ph.D. Mie University Graduate School of Medicine

2. Professional Training and Employment:
2007-2011: Associate Professor, Mie University Hospital
2011-2013: Visiting Researcher, Post Doctor Fellow, Baylor Medical Center at DALLAS
2013-2016: Associate Professor, Department of Gastrointestinal and Pediatric Surgery
2018-2020: Associate Professor, Department of Gastrointestinal and Pediatric Surgery
2020-: Professor, Department of Gastrointestinal & Pediatric Surgery, Division of Clinical Sciences, Mie University Graduate School of Medicine
2022-: Professor, Department of Innovative Surgery and Surgical Techniques Development, Division of Clinical Sciences, Mie University Graduate School of Medicine

3. Board certification
- Japan Surgical Society
- The Japanese Society of Gastroenterological Surgery
- The Japanese Society for Coloproctology
- The Japanese Society of Gastroenterology
- The Japanese Gastroenterological Association
- The Japanese Society for Hereditary Tumors
- Japanese Society for Abdominal Emergency Medicine
- Japanese Board of Cancer Therapy
- Infection Control Doctor
- American College of Surgeons Fellow (FACS)

4. Research Fields
His attention has focused on colorectal surgery with bowel function and organ preservation for the patients with colorectal cancer and inflammatory bowel disease as well as perioperative management for the goal of decreasing surgical complications.

Notable achievements of his research are the molecular biology of colorectal cancer and inflammatory bowel disease to understand the genetic and epigenetic mechanisms involved in the development and progression of these diseases. His work shed light on the underlying factors contributing to the aggressive nature of these diseases and paved the way for potential diagnostic and therapeutic interventions.

5. Bibliography
- English articles: 307 papers, First Author: 50 papers
- Representative first author’s papers:
Long-term Outcomes of Endoscopic Resection in T1 Colorectal Cancer and Strategies for Determining Additional Surgery

Yunho Jung
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Introduction: Colorectal cancer (CRC) is the third or fourth commonest cancer worldwide. Some of the CRCs, which were treated only by surgery, are increasing in frequency of being treated with endoscopic procedures such as endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD). However, since Lymph node metastasis (LNM) is observed in some T1 CRC cases, it is essential to consider the possibility of LNM before deciding on endoscopic and surgical treatment. In this chapter, I’d like to discuss the long-term outcome after endoscopic treatment in T1 CRC.

Histological classification and LNM: Depth of invasion into the submucosa and deeper colonic layers based on pathological assessment have been described according to different classification methods such as TNM staging, Hayegit, and Kituch systems. According to “TNM staging” of CRC, T1 means the malignant cells invade through the muscularis mucosae into the submucosa but do not breach the muscularis propria.1 The incidence of LNM was reported to be 6.8-17.8% in T1 CRC.2

Recommendation by current guidelines: The indication criteria for surgical resection as an additional treatment after endoscopic resection of T1 CRC have been defined in the Korean,3 Japanese,4 and United States guidelines.5 Surgical resection with lymph node dissection is recommended if any of the following findings is observed: (1) positive vertical margin, (2) depth of submucosal invasion≥100µm; (3) positive lymphovascular invasion; (4) poorly differentiated adenocarcinoma, signet-ring cell carcinoma, or mucinous carcinoma; (5) Tumor budding (BD2/3).

Comparison of Outcomes of Endoscopic resection vs surgery: A population-based study of 13,157 patients reported no difference in the 5-year survival rate between endoscopic resection and surgical treatment for early-stage colon cancers located in the left colon regardless of size and right-sided lesions that were <2 cm; however, surgical resection had greater survival in comparison to endoscopic resection (20–39 mm: 91.6 vs 74.2%; ≥40 mm: 92.4 vs 60%);6 Similarly, Mournier et al also reported no difference in 5-year colorectal cancer-specific recurrence-free survival rates (97.6% vs 97.5%; p=0.75) between endoscopic resection and surgical resection of T1 colorectal tumors.7

Conclusions: When endoscopic removal was performed based on the current guidelines considering the possibility of LNM metastasis for T1 CRC, the long-term outcome does not appear to be inferior to surgical removal. After endoscopic removal of T1 CRC, it is considered important to establish additional surgery plans or appropriate follow-up plans based on histological results.

References

Curriculum Vitae

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Professional Career:
2009.5.–2010.3. Clinical fellowship in Soonchunhyang University Hospital (Division of Gastroenterology)
2010.7.–2012.6 Research fellowship in Beth Israel Deaconess Medical Center, Harvard Medical School (Division of Gastroenterology)
2012.7. – Professor in Soonchunhyang University Cheonan Hospital (Gastroenterology)

Main Interests:
Colorectal disease
Endoscopic resection techniques in gastrointestinal tract
Inflammatory bowel disease

Publications:
Adding bevacizumab to neoadjuvant chemoradiotherapy increases pathological complete remission and survival in patients with locally advanced rectal cancer

Jason Chia-Hsien Cheng, Yun Chiang, Jin-Tung Liang
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Purpose: This retrospective study investigated the impact of adding bevacizumab to neoadjuvant chemoradiotherapy (NCRT) in patients with locally advanced rectal cancer (LARC).

Methods: This retrospective study enrolled patients with LARC undergoing NCRT with or without bevacizumab followed by curative resection at National Taiwan University Hospital from 2009 to 2021. Locoregional recurrence was defined as recurrence within the irradiated field and distant metastasis as outside the irradiated field. Associations between clinical factors and pathological complete remission (pCR), overall survival (OS), locoregional recurrence-free survival (LRFS), and distant metastasis-free survival (DMFS) were analyzed using ANOVA and Cox proportional hazards model. Propensity score matching (PSM) analysis was used to evaluate the effects of adding bevacizumab. Programmed death-ligand 1 (PD-L1) immunostaining on rectal tumor biopsies taken at diagnosis was conducted to assess the correlation between PD-L1 expression level and treatment response.

Results: A total of 200 patients were enrolled. Of these, 39 patients (18/54 vs. 21/146 without bevacizumab, p=0.004) achieved pCR. Patients receiving bevacizumab had more T4 disease (p=0.005), low-lying rectal tumor (p=0.047), concurrent oxaliplatin use (p<0.001), but less frequent adjuvant chemotherapy (p=0.005). With a median follow-up of 71 months, 5-year OS, LRFS, and DMFS were 86%, 84%, and 79%, respectively. Factors associated with pCR in univariate analysis were clinical N0 (cN0), gross tumor volume ≤70 ml, and adding bevacizumab. In multivariate analyses, cN0 and adding bevacizumab remained significantly associated with pCR, and pCR was the only independent factor for OS (HR=0.32, p=0.004), DMFS (HR=0.29, p<0.0001), and LRFS (HR=0.32, p=0.002). In PSM cohort, adding bevacizumab was associated with better OS (p=0.034) and DMFS (p=0.045). A high PD-L1 expression, as determined by the VENTANA PD-L1 (SP263) assay, was associated with pCR rate only in patients receiving the additional bevacizumab.

Conclusions: Adding bevacizumab to NCRT in LARC patients contributes to improved survival by increasing pCR with tolerable toxicities. A correlation might exist between immunochemo PD-L1 expression level and the response to bevacizumab.

Curriculum Vitae

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EDUCATION
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Jason Chia-Hsien Cheng, M.D., M.S., Ph.D., FASTRO (成佳憲)
Colonoscopy for colorectal cancer screening and management of early colorectal cancer

Masau Sekiguchi
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Screening, and treatment of precancerous lesions and early colorectal cancer (CRC) are essential to lower the mortality of CRC, and colonoscopy plays an important role. Population-based CRC screening using a fecal immunochemical test followed by colonoscopy has been implemented since 1992 in Japan; however, CRC remains a leading cause of cancer-related deaths. Considering the potential effectiveness and cost-effectiveness of screening colonoscopy, discussions about more efficient use of colonoscopy in CRC screening are warranted (Sekiguchi M, et al. Jpn J Clin Oncol. 2016;46:116-125). Risk-stratification of the screening population and the possibility of using computer-aided detection systems for screening colonoscopy also warrant discussion (Sekiguchi M, et al. J Gastroenterol. 2018;53:1109-1119). Sekiguchi M, et al. Dig Endosc. 2023;10.1111 [published online ahead of print]). Regarding the treatment of early CRC, endoscopic submucosal dissection (ESD) has become the standard treatment method for large cTis and T1a cancers. Compared to piecemeal endoscopic mucosal resection, ESD is more acceptable for large lesions in terms of effectiveness and cost-effectiveness (Sekiguchi M, et al. Dig Endosc. 2022;34:553-568). Despite the remarkable development of endoscopic diagnosis, pT1b cancers occasionally occur after endoscopic resection. The current standard management methods for pT1b cancer is colectomy with lymphadenectomy; however, whether such surgical treatment could be performed in patients at risk for operative complications, such as elderly patients, is difficult to determine. The optimal management of such patients requires discussion among a multidisciplinary team (MDT). Data for prediction of the risk of lymph node metastasis from T1 CRC is useful for this decision (Kajiwara Y, et al. Gastrointest Endosc. 2023;97:1119-1128). A single-arm confirmatory trial of adjuvant chemoradiation for patients with high-risk rectal submucosal invasive cancer (JCOG1612) is ongoing to establish less invasive management. A new clinical trial for pT1b colon cancer is also warranted. A single-arm phase III confirmatory trial on indications of ESD for elderly patients with early gastric cancer (JCOG1902) is being conducted, and it may also be meaningful to examine the potential for expanding the indications of colorectal ESD for elderly patients (Sekiguchi M, et al. Jpn J Clin Oncol. 2022;52:425-432). The difficulty of managing rectal neuroendocrine tumors following endoscopic resection is another hot topic, and an MDT approach and further investigations are key to solve this issue (Sekiguchi M, et al. J Gastroenterol. 2022;57:547-558).

Curriculum Vitae

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Recent major publications:
Recent advances in multidisciplinary treatment for colorectal cancer

Hyun Seok Lee
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Colorectal cancer (CRC) is the third most common cancer type and the second cause of cancer-related mortality in the analysis of global cancer statistics. Stage IV colorectal cancer (CRC) has heterogeneous characteristics in tumor extent and biology. The overall survival of patients with metastatic CRC has improved with the development of multimodal treatments and new chemotherapeutic drugs. Resection of metastatic CRC is recommended when the metastatic lesions are technically present for complete removal. Before determining the resection of metastatic sites, the resectability and usefulness of locoregional surgical treatment for metastatic CRC should be fully assessed with consideration of the radiologic evaluation and the patient’s condition. In addition, clear surgical margins and technical assurance for complete resection of metastatic sites should be ensured before the surgery. Resection of metastatic CRC is performed for liver, lung, or peritoneal metastases.

Synchronous liver and primary tumor resection can be considered in patients with adequate conditions. Treatment strategies for patients with synchronous liver and CRC should be considered in conjunction with a thorough evaluation of metastatic lesions and primary tumor stages.

Solitary pulmonary metastatic lesions can be considered for surgical resection using video-assisted thoracic surgery (VATS) or open thoracotomy metastasectomy. Currently, VATS is commonly used to treat solitary pulmonary metastasis. Local ablation with radiotherapy can be used to treat lung metastasis. With the development of modern systemic chemotherapy, the treatment of pulmonary metastasis requires multidisciplinary approaches combined with surgical resection and radiotherapy and the use of accurate diagnostic imaging tools.

In the treatment of patients with CRC with peritoneal metastasis, cytoreductive surgery with hyperthermic intraperitoneal chemotherapy can be considered. Complete surgical resections and the development of adequate chemotherapeutic agents for use against peritoneal metastatic lesions are required to prolong survival and increase treatment efficacy in patients with CRC with peritoneal metastases. Surgical treatments should be performed in patients with symptomatic primary tumors with unresectable metastases. However, primary tumor resection in patients with asymptomatic CRC with synchronous, unresectable metastases did not show overall survival benefits in recent studies. Therefore, the treatment of metastatic CRC is challenging due to the variable tumor extent and heterogeneous characteristics. The location and extent of metastatic lesions should be considered to treat patients with stage IV CRC. Adequate surgical treatments at the appropriate time can improve survival and prevent tumor-related complications. Tailored surgical treatments and multidisciplinary approaches may improve survival and the quality of life in patients with metastatic CRC.

Curriculum Vitae

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EDUCATION
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March 2013 – March 2018: Assistant professor of Division of Gastroenterology and Hepatology in Kyungpook National University Hospital
Feb. 2010 – March 2013: Fellowship of Gastroenterology & Hepatology in Kyungpook National University Hospital
March 2006 – Feb. 2010: Residentship of Internal Medicine in Kyungpook National University Hospital
March 2002 – Feb. 2003: Internship in Kyungpook National University Hospital, Daegu, Korea

SELECTED PUBLICATIONS (recent 20)
Role of endoscopic muscular dissection for rectal cancer with clinical complete response after concurrent chemoradiotherapy

Chao-Wen Hsu¹, Chu-Kuang Chou², Jen-Hao Yeh³

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Background
For clinical T2N+/- or T3N+/- rectal cancer, concurrent chemoradiotherapy (CCRT) followed by radical low anterior resection (LAR) +/- diversion stoma is the standard treatment modality. The clinical complete response (cCR) rate after CCRT can achieve 10-20% based on the modern total neoadjuvant therapy (TNT) and neoadjuvant chemotherapy. Endoscopic muscular dissection (EMD) for cCR rectal cancer after CCRT, may play a diagnostic role to decide watch & wait (WW) or radical LAR in carefully selected patients. We retrospectively evaluated the technical feasibility and the short-term outcome of EMD for rectal cancer with cCR after CCRT.

Methods
A retrospective chart review of cases of EMD for rectal cancer with cCR after CCRT from Jan 2022 to Aug 2023 at our institution was performed. Clinical factors and imaging, procedural, and pathology results were collected and analyzed.

Results
Eight EMD for rectal cancer with cCR were performed. Before CCRT, 6 of lesions were initially clinically staged as T2-3N0 and 2 were T3N1. The en-bloc resection rates and R0 resection were 100% without complications. Six lesions had pathologically complete response (pCR), 1 lesion had morphologically changed to adenoma and 1 lesion had minimal residual ypT1. No patients received subsequent radical LAR in this cohort.

Conclusions
EMD for rectal cancer with cCR after CCRT is technically feasible with low complication rates. There may be a diagnostic role in EMR in assessing pathologic response after CCRT and a potentially therapeutic role to avoid radical LAR in carefully selected patients.

Curriculum Vitae

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EXPERIENCE
2022 Director of SOCIETY OF COLON AND RECTAL SURGEONS, Taiwan.
2023 Fellowship in NTT medical center, Tokyo
2014 Fellowship in University of Washington, Seattle, USA
2012 Fellowship in National cancer center, Tokyo

Academic qualifications
1996 – 2003 School of medicine, National Yang-Ming University, Taiwan

Certificate:
Board of Surgery, Taiwan
Board of Colorectal surgery, Taiwan

Expertise
Advanced Endoscopic treatment
Endoscopic submucosal dissection
Minimal invasive colorectal surgery

Invited speaker
1. Invited speaker in international colorectal forum 2015, Taichung, Taiwan
2. Invited speaker in APDO 2016, Kobe, Japan
3. Invited speaker in international colorectal forum 2019, Taiwan
4. Invited speaker in international colorectal forum 2020, Taiwan
5. Invited speaker in international colorectal forum 2021, Taiwan
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7. Invited speaker in international colorectal forum 2022, Taiwan
8. Invited speaker in APFCP 2023, Taiwan

Publication
Upper GI
Multimodal treatments for esophagogastric junction cancer

Chair (J): Hiroya Takeuchi
Hamamatsu University School of Medicine, Japan

Chair (K): Jae Gyu Kim
Department of Internal Medicine, Chung-Ang University College of Medicine, Korea

Chair (T): Chi-Yang Chang
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Discusser (J): Takaki Yoshikawa
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Discusser (K): Hwoon-Yong Jung
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Speaker (J): JKT2-1
Neoadjuvant chemotherapy and conversion surgery for EGJ adenocarcinoma
Yu Imamura
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Speaker (K): JKT2-2
Minimally invasive surgery for gastrooesophageal junction adenocarcinoma
Jin-Jo Kim
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Speaker (T): JKT2-3
Exploring the feasibility of endoscopic management for T1b esophageal cancer
Chu-Kuang Chou
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Rising Star Program (J): JKT2-RS1
Approach and therapeutic value index for Siewert type 2 esophagogastric junction adenocarcinoma
Eisuke Booka
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Rising Star Program (K): JKT2-RS2
Endoscopic treatment for esophagogastric junction carcinoma
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Rising Star Program (T): JKT2-RS3
Recent advances in perioperative treatment for esophagogastric junction cancer
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Neoadjuvant chemotherapy and conversion surgery for EGJ adenocarcinoma

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Background and Aim: Adenocarcinoma of the esophagogastric junction (EGJ) is an aggressive tumor, and curative resection (R0) rate is not sufficient. It has been unclear whether conversion surgery is beneficial in the patient with initially unresectable tumor. Here, focusing on Siewert type I-II cases who needed thoracic approach, and we report 1) a multicenter phase II study of SOX (S-1 + oxaliplatin) therapy as a NAC, and 2) the clinical indication of conversion surgery.

Methods: 1) cT3/4a and/or cN+ cases with 3cm or longer esophageal invasion was eligible. The primary endpoint was R0 resection rate, and the planned sample size was 50 cases based on an expected R0 resection rate of 85% (at the threshold of 70%), with a one-sided alpha of 0.1 and power of 80%. 2) Among 438 cases with Siewert type I/II tumors who were treated at our institution, 95 patients with initially unresectable tumors were examined.

Results: 1) Fifty patients were enrolled between June 2016 and April 2020. The overall response rate (CR/PR was 0/9, respectively) was 18% (95%CI, 8.6-31.4%). SOX-related grade 3-4 adverse events (AEs) occurred in 6 cases. R0 resection rate was 86.0% (95%CI, 73.3-94.2%). Histopathological examination revealed that grades 3/2/1a/1b/not-evaluated was observed in 9/6/8/21/4 (due to R2 resection), and pathological complete response rate was 18% (95%CI, 8.6-31.4%). 2) Conversion surgery was successfully performed by transthoracic (N=12) or transhiatal approach (N=5), and remaining 60 cases continued chemotherapy (unresected cases). In conversion cases with thoracic approach (N=12), half of those were treated by chemotherapeutic regimen including Trastuzumab (N=5) or Nivolumab (N=1). Compared to the unresected cases, trastuzumab was frequently administered in conversion cases (conversion 50%, unresected 27%), and conversion cases experienced favorable outcomes [3-yr overall survival (OS) after initial treatment; conversion 81.5% vs. unresected 12.7%, P=0.0002].

Conclusions: Neoadjuvant SOX met the primary endpoint of R0 resection rate 86% (>70%), with acceptable adverse events. Conversion surgery conferred prolonged overall survival in the patient with initially unresectable EGJ adenocarcinoma. HER2 overexpression may be a useful biomarker for conversion surgery.

Curriculum Vitae

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Education:
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April 2006-March 2010

Professional Training and Employment:
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July 2003 Department of Surgery, Japanese Red Cross Kumamoto hospital
July 2005 Department of Surgery, Kumamoto city hospital
April 2010 Resident in Department of Gastroenterological Surgery, Kumamoto University
December 2010 Research Fellow in Department of Medical Oncology, Dana-Farber Cancer Institute/ Harvard Cancer Center, U.S.A.
May 2013 Resident in Department of Gastroenterological Surgery, Kumamoto University
June 2013 Assistant Professor in Department of Gastroenterological Surgery, Graduate School of Medical Sciences, Kumamoto University → May 2023 Visiting Associate Professor
April 2014 Assistant Professor in Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University
April 2015 Resident in Division of Gastroenterological Surgery, The Cancer Institute Hospital of Japanese Foundation of Cancer Research (JFCR)
May 2017 Associate in Division of Esophageal Surgery, Department of Gastroenterological Surgery and Center for Development of Advanced Cancer Therapy, The Cancer Institute Hospital of JFCR
June 2019 Head in Division of Esophageal Surgery, Department of Gastroenterological Surgery, The Cancer Institute Hospital of JFCR

Awards:
2014 JSGS Young Investigator of the Year 2014
2016 Poster Award, 89th Annual meeting of the Japanese Gastric Cancer Association
2017 Research Award, 89th Annual meeting of the Japanese Gastric Cancer Association
2018 Young Investigator Award, The 11th The International Gastrointestinal Consensus Symposium (IGICS)
2019 Poster Walk, 2019 ASCO GI
2020 Poster Highlight, 2020 ASCO-GI
2021 Research Award, 10th Annual meeting of Japanese Society for Gastroenterological Carcinogenesis
2021 The Best Citation Award, The Japanese Gastroenterological Association
2022 15th Research Award, Japanese Society of Clinical Pharmacology and Therapeutics
Minimally invasive surgery for gastroesophageal junction adenocarcinoma

Jin-Jo Kim
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Gastroesophageal junctional cancer (GEJc) is defined as adenocarcinoma with an epicenter within 5 cm of the GEJ and extending into the esophagus. The incidence of GEJc has increased substantially in the past few decades, even in Eastern countries. GEJc is usually classified into 3 categories according to the Siewert system, which is based on the location of the epicenter of the tumor. Among these, Siewert type II tumors, located 1 cm above to 2 cm below the GEJ, represent true carcinoma of the GEJ.

According to the recent prospective trial in Japan, lower mediastinal lymph node dissection (LND) should be performed when the length of esophageal invasion is 2 cm or more. If the length is more than 4 cm middle and upper mediastinal LND should be performed, together. In the former case, Japanese researchers recommend to perform number 110 lymph node (LN) only. However, the anatomical landmark among the lower mediastinal LNs (No. 110, 111 and 112) is vague and it is difficult to differentiate one from the others. In my opinion, it would be easier and better to dissect the lower mediastinal LN as a whole. Moreover, systematic lower mediastinal LND would offer a clearer surgical view in later anastomosis in the lower mediastinum.

Recent laparoscopic transhiatal approach has some advantages over the open counterpart. Surgical view and instrumentation are much better in laparoscopic approach. I think this approach will have a promising future in this field.

In order to perform laparoscopic transhiatal LND, mobilization of Lt. lateral section of liver is essential to obtain a good surgical view. After full mobilization of Lt. lateral section, it is folded toward right side through a hole made in falciform ligament. An anterior midline incision is made on the diaphragm and the hiatal opening is widely opened. Lower mediastinal LND is performed through this hole. First, supradiaphragmatic LN (No. 111) is dissected and bilateral pulmonary ligaments (No. 112 pul) and anterior side of the descending aorta (No. 112 aoA) are dissected to the level of inferior pulmonary vein. After lower mediastinal LND, the esophagus is cut at the level of 2 cm above the upper border of the tumor and the proximal stomach and upper abdominal LNs including No. 7, 8a, 9, 11p, 19 and 20 are resected. And then esophagogastrostomy using double flap technique is proceeded in the lower mediastinum.

Curriculum Vitae

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Education:
M.D. Degree, Korea (1994)
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PROFESSIONAL SOCIETY MEMBERSHIP & CURRENT ACADEMIC ACTIVITY:
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Editor-in-Chief, The Korean Journal of Gastrointestinal Surgery
Director, Ethical Committee, The Korean Society for Bariatric and Bariatric Surgeons
Steering Committee, Korean Laparoscopic Gastrastestinal Surgery Study Group
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Exploring the feasibility of endoscopic management for T1b esophageal cancer

Chu-Kuang Chou

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Based on data from the Taiwan cancer registry, the overall crude incidence rate of esophageal cancer in 2020 was reported to be 12.19, and this rate has remained stable over the past decade in Taiwan. The majority of esophageal cancer cases are of squamous origin, while adenocarcinoma from the esophagogastric junction (EGJ) constitutes 4.21-4.79% of cases. Among all esophageal cancer cases, 9.24% were classified as clinical stage 1, and 14.49% were categorized as pathologic stage 1.

The advancement and acceptance of endoscopic resection have led to a shift in the management of early EGJ cancers, moving away from surgery or concurrent chemoradiation therapy (CCRT) and towards endoscopic treatment. En-bloc resection using endoscopic submucosal dissection (ESD) has become a crucial approach for EGJ lesions with suspected superficial invasive cancers. The management of squamous cell carcinoma near the EGJ in Taiwan closely mirrors that of squamous cell carcinoma at other sites in the esophagus. As for adenocarcinoma, the en bloc resection rate for ESD in esophageal adenocarcinoma is higher than that of endoscopic mucosal resection (EMR). ESD is considered the preferred treatment for elevated lesions and those with potential invasive cancers, allowing endoscopists to obtain a definitive diagnosis. Nonetheless, managing submucosal invasion cancers remains challenging. The Japan Gastroenterological Endoscopy Society 2020 guideline for Endoscopic submucosal dissection/endoscopic mucosal resection in esophageal cancer suggests that pT1b esophageal adenocarcinoma should be considered for surgical resection. The European Society of Gastrointestinal Endoscopy 2022 guideline suggests that Barrett’s esophagus-associated superficial cancers with superficial submucosal invasion, showing well to moderate differentiation and lacking lymphovascular invasion, can be effectively treated endoscopically. Additionally, a clinical update on T1b Esophageal Cancer in the United States in 2019 reported a low risk (6% metastasis rate) of lymph node metastasis in esophageal adenocarcinoma with submucosal invasion <500 µm. The management of pT1b esophageal adenocarcinoma should take into account the risk of lymph node metastasis and carefully weigh the risks and benefits of additional surgery or concurrent chemoradiation therapy. Further research and data collection are essential to strengthen the existing body of evidence. In this section, we aim to provide an in-depth review of the current evidence and share our institution’s case experience concerning T1b EGJ cancer.

Curriculum Vitae

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Academic Degree
Medical doctor, College of Medicine, National Taiwan University
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Specialist, Gastroenterological Society of Taiwan
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Publications
Approach and therapeutic value index for Siewert type 2 esophagogastric junction adenocarcinoma

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[Background] Based on the metastasis rate from a prospective observational study on esophagogastric junction adenocarcinoma, the range of lymph node dissection and the surgical approach are recommended according to esophageal involvement, however the therapeutic value index is unclear.

[Patients and Methods] From January 2016 to June 2022, 55 patients who underwent surgery for Siewert type 2 esophagogastric junction adenocarcinoma were investigated for the metastasis rate of mediastinal/abdominal lymph nodes, therapeutic value index = metastasis rate * 5-year OS rate in patients with metastasis, and short-term outcomes of right thoracic / transhiatal approach.

[Results] When divided into 41 cases of the right thoracic approach (Group A) and 14 cases of the transhiatal approach (Group B), tumor size (50mm vs 24mm) and esophageal involvement (30mm vs 12.5mm) were significantly longer in Group A. The degree of progression (cStage1/2/3/4) was significantly higher in Group A (7/6/26/2) compared to Group B (5/7/2/0). The operation time (524 minutes vs 359 minutes) and blood loss (215ml vs 75ml) were significantly less in Group B, however there was no significant difference in pneumonia (9.8% vs 7.1%), anastomotic leakage (9.8% vs 0%), and pancreatic fistula (2.4% vs 0%) between the two groups. The therapeutic value index was #1 (18.7), #2 (26.4), #3a (20.3), #7 (21.0), #8a (0), #9 (11.4), #11p (4.2), #110 (8.5), #105 (0), #106recR (0), #108 (0), with the therapeutic value being high for abdominal lymph nodes (#1, #2, #3a, #7, #9) and lower mediastinal lymph nodes (#110), however the therapeutic value was low for #8a, #11p and upper mediastinal lymph nodes.

[Conclusion] For Siewert type 2 esophagogastric junction adenocarcinoma, the therapeutic value of upper mediastinal lymph nodes dissection is low, and adequate lymph node dissection of the abdomen and lower mediastinum and safe reconstruction according to the esophageal involvement are desirable.
Endoscopic treatment for esophagogastric junction carcinoma

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Superficial esophageal cancer (SEC) is frequently detected by a screening endoscopy and the development of endoscopic imaging techniques facilitate the early diagnosis. Endoscopic resection (ER) has been used for SEC when there is a negligible risk of lymph node metastasis (LNM). The majority of esophageal cancers are squamous cell carcinomas (SCCs) in the Asia. SCC occurs more often in the upper and middle third of the esophagus. Esophageal adenocarcinoma mainly develops in the lower third and at the esophagogastric junction (EGJ). The global incidence of EGJ cancer has increased in recent years. From an anatomical and histopathological point of view, EGJ represents the boundary between the esophagus and stomach. Fortunately, ER is established as the first choice treatment for early EGJ carcinoma without histopathologic risk factors of LNM. Multiple studies and long-term analyses have demonstrated excellent efficacy and safety of ER as an alternative to surgery for these lesions. Nevertheless, after ER of EGJ carcinoma with histopathologic risk factors for LNM, optimal management is still unclear.

Curriculum Vitae

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Educational Background
2003 B.S., Sungkyunkwan University School of Medicine, Seoul, Korea
2008 M.S., Graduate School, Sungkyunkwan University, Seoul, Korea
2015 Ph.D., Graduate School, Sungkyunkwan University, Seoul, Korea

Professional Career
2015 - Assistant Professor
Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, Korea
2021 - Associate Professor
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Research Field
Endoscopic interventions
Esophageal cancer
Esophageal motility disorders

Recent Papers
Recent advances in perioperative treatment for esophagogastric junction cancer

KuoHsing Chen
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The incidence of esophagogastric junction (EGJ) cancer is increasing worldwide. EGJ cancer is defined as the epicenter of adenocarcinoma located within 5 cm of EGJ according to Siewert classification, or any histology of cancer with epicenter withing 2 cm of EGJ based on the Nishi classification in Japan. The prognosis of EGJ cancer is poor compared to gastric cancer and establishing optimal treatment strategies is important.

Currently, few clinical trials are designed for EGJ cancer only because EGJ cancer is still a less frequently occurring tumor type, especially in Asia. EGJ cancer patients are usually enrolled in clinical trials for esophageal or gastric cancer patients. Thus, we can only try to identify the advance of anti-cancer treatments in EGJ cancer from these trials. Recently, development of multimodal treatments with perioperative strategy has improved the treatment outcomes in locally advanced EGJ and gastric cancer, such as novel chemotherapy combinations, chemoradiation, targeted therapy and immune checkpoint inhibitors. A pivotal trial demonstrated perioperative FLOT4 increased the survival outcomes compared to ECF in Western patients. The initial results from two clinical trials (KEYNOTE 585 and MATTERHORN) show immune checkpoint inhibitor plus chemotherapy is associated with higher pathological complete response rate compared to chemotherapy alone. Biomarker-driven strategy has also been tested in several trials in Her2 amplified and mismatch repair deficient or microsatellite instability-high tumors and the results are also encouraging. In this presentation, I will have a mini-review of the recent advance of perioperative treatment in EGJ cancer.

Curriculum Vitae

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Department of Medical Oncology, National Taiwan University Cancer Center, Taipei, Taiwan

EDUCATION
Taipei Medical University, Taipei, MD. July, 1998- June, 2005
Graduate Institute of Oncology, National Taiwan University College of Medicine, July, 2015- Jan, 2023

PROFESSIONAL EXPERIENCES
Attending physician: Department of Medical Oncology, National Taiwan University Cancer Center. March, 2019- present.
Attending physician: Department of Oncology, National Taiwan University Hospital, Taipei, Taiwan. July, 2015- March, 2019
6th Clinical Research Skill Advancement Workshop (J-HOPE), Chiba, Japan, 2017
3rd Paul Carbone Academy, Taipei, 2013-2014
Attending physician: Oncology Department of National Taiwan University Hospital, Yun-Lin Branch. July, 2013- June, 2015
Fellowship: Oncology Department of National Taiwan University Hospital. July, 2010- June, 2013
Resident: Internal Medicine Department of National Taiwan University Hospital. July, 2007- June, 2010

LICENSES / CERTIFICATION License: National Board of Medicine, 2005
Certification: Board of Internal Medicine, 2010
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FIELDS OF INTERESTS
Colorectal Cancer, Gastric Cancer, Epigenetics, Immuno-oncology

PUBLICATIONS (within 5 years):
| JKT3-RS1 | Clinical outcomes of EUS-guided antegrade stone removal for common bile duct stones in patients with surgically altered anatomy | Shuntaro Mukai | Department of Gastroenterology and Hepatology, Tokyo Medical University, Japan |
| JKT3-RS2 | Current status and future perspectives of Interventional EUS in Asia focused on EUS-guided gallbladder drainage in South Korea | Se Woo Park | Department of Internal Medicine, Hallym University Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong, South Korea |
| JKT3-RS3 | Radiofrequency ablation: A novel endoscopic focal treatment of pancreatic cancer | Meng-Ying Lin | Department of Internal Medicine, National Cheng Kung University, Tainan, Taiwan |
Interventional EUS has made dramatic progress in Japan since EUS-FNA was covered by insurance in 2010. In Japan, there was a negative opinion about FNA due to the high level of trust in imaging diagnosis and the risk of needle tract seeding caused by puncture of malignant tumors. After reports on the usefulness of neoadjuvant treatment (NAT) for pancreatic cancer, there is a growing consensus that it is necessary to obtain histological confirmation by FNA. In addition, there have been many reports on the high histological diagnostic capability of FNA, as well as biomarker and gene evaluation, and FNA has become a well-established technique. However, there are many reports from Japan of needle tract seeding after FNA, and many institutions still consider that FNA is contraindication for cystic pancreatic tumors.

In terms of therapeutic indication, drainage of pancreatic cysts has been performed and the indications have expanded to include drainage of the biliary tract and pancreatic ducts, etc. In 2019, the guideline for EUS-BD was published in Japan, which have contributed greatly to the safe technique of interventional EUS. EUS-guided drainage requires several steps such as puncture, dilation, and stent deployment. In the past, without dedicated devices for interventional EUS made the procedure was challenging, and several serious adverse events were reported. Recently, dedicated dilation devices such as mechanical dilators, cautery dilators, and drill-type dilators, have been developed and are now available to use in Japan. In addition, specialized stents that can be easily deployed are also commercially available. The development of specialized devices is considered to have made it possible to perform the procedure more safely and reliably. Lumen apposing metal stent (LAMS) is now covered by medical insurance for use in peri-pancreatic fluid collection (PFC) in Japan. LAMS can be used only for PFC, and the indication has not been expanded to the gallbladder drainage. Interventional EUS will continue to progress in Japan, but it is unlikely that all procedures will replace ERCP. The education program is required to perform for the safe interventional EUS procedures.
Development and Clinical Application of a Novel Stent for EUS-Guided Transmural Drainage

Lee Sang Hyub
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Endoscopic ultrasonography-guided transmural drainage in the pancreatobiliary field is currently widely used for acute cholecystitis in peripancreatic fluid retention, and has shown great progress in recent years. In the past, a dedicated stent for this procedure was not developed, so a plastic stent was inserted into the biliary tract or a tubular metal stent (tubular SEMS) was used. However, tubular SEMS has the disadvantage of low patency and technical difficulty in insertion, and tubular SEMS has the disadvantage of high risk of deviation and possible leakage. Recently, LAMS (Lumen Apposing Metal Stent) was developed as a stent for endoscopic ultrasound-guided transmural drainage to improve these disadvantages. LAMS is a barbell-shaped stent with a very large diameter and short length, and has the advantage of lowering the risk of stent detachment or leakage by bringing the two structures into close contact. It is considered to be superior to conventional stents in pancreatic fluid retention with solid debris as it is advantageous for endoscopic debriement. (1,2) However, for endoscopy beginners with insufficient experience, LAMS procedures are technically difficult, and when stents are placed for a long period of time, there is a risk of adverse reactions such as bleeding or buried LAMS syndrome (3). In the 2018 European Society of Gastrointestinal Endoscopy (ESGE) guidelines, when LAMS is inserted in pancreatic duct break syndrome, it is recommended to remove it within 4 weeks to prevent adverse reactions (4). Tornado stent was developed to overcome these disadvantages. The Tornado stent is a self-expanding, self-expanding, self-expanding metal stent with a double pigtail structure, and is composed of a silicon coating with a metal thread of nitinol (5). The characteristic pig tail structure on both ends is in the form of a flexible spiral, which is designed to minimize the risk of proximal or distal stent detachment. The diameter of the stent is 8 mm, and the length is 22 cm when inside the delivering catheter, 14 cm when the outer sheath is removed during deployment, and 6 cm after the stent is fully deployed and has a spiral shape. Through this design, it is expected that the disadvantages of existing stents can be supplemented. Compared to plastic stents, it has a wider diameter, enabling effective drainage. Compared to tubular SEMS, the flexible spiral pigtail structure reduces the risk of stent detachment. Compared to LAMS, the stent is more flexible, making it easier to remove the stent after fistula formation and the risk of serious adverse events such as buried LAMS syndrome or hemorrhage is expected to be low. Recently, an animal experiment was conducted to evaluate the feasibility and safety of ultrasound-guided transmural drainage using a tornado stent. Eight mini pigs (Sus Scrofa) underwent gastro-cholecystectomy using Tornado stent under ultrasound endoscopic guidance, and were followed up for 28-49 days. Technical success was confirmed in all 8 test animals, and patency of the stent was confirmed in all 8 animals in follow-up endoscopy after 28-49 days, and the stent could be easily removed using a snare. There were no adverse reactions such as stent detachment, and a microscopic endoscope was inserted through the fistula to enter the gallbladder. Recently, the use of the Tornado stent has begun in clinical practice, and in the near future, it is expected that the range of use will be expanded to clinical studies to prove its role as a stent in lowering the risk of complications in ultrasound-guided transmural drainage.

References

Curriculum Vitae

Lee Sang Hyub
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Education and Training
2005 – 2007: Ph.D. in Medicine
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Professional Experiences
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2015-2016: Visiting Scholar
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2012 – 2013: Assistant professor
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Field of expertise:
I am a gastroenterologist and an endoscopist of pancreaticobiliary disease such as acute pancreatitis, chronic pancreatitis, pancreatic cancer, gallstone and bile duct cancer. I assumed my present appointment in 2019 and currently share responsibility for the gastroenterological services in the Seoul National University Hospital. These include the full range of diagnostic procedures, clinics including chemotherapy and consultations appropriate to a large teaching hospital. I have had particular responsibility for biliary and pancreatic diseases. I have performed the clinical and translational study for biliary and pancreatic diseases. I am going to develop the new type stents for the intervention and new therapeutic agent for the pancreate-biliary malignancy.

My research topics:
- Pancreas and Bile Duct Cancer
- Cholangitis, Pandreatitis, Choledocholithiasis
- Therapeutic Endoscopy using ERCP and EUS
- Development of New Device and Stent
- Translational Research using Pancreatic Cancer Organoid

Publications:
109 international journal as 1st and Corresponding Author
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Endoscopic ultrasound-guided gastroenterostomy with a lumen-apposing metal stent: a multicenter prospective study

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Gastric outlet obstruction (GOO) can be caused by periampullary malignancies and often leads to a reduction in a patient’s quality of life. Recently, endoscopic ultrasonography-guided gastroenterostomy (EUS-GE) using a lumen-apposing self-expandable metal stent (LAMS) has been developed as a minimally invasive and durable endoscopic treatment for GOO. EUS-GE has the advantage of being minimally invasive as an endoscopic procedure and EUS-GE could provide long-lasting effects with lower recurrence rates. Moreover, a recent study suggests that EUS-GE has similar technical and clinical success rates compared to laparoscopic gastroenterostomy. Interestingly, EUS-intervention seems to reduce the length of stay and incidence of AEs, suggesting possible advantages compared to surgery.

In our prospective study including 139 patients, technical and clinical success was achieved in 136 patients (97.8%) and 129 (92.8%), respectively. The mean change in the gastric outlet obstruction scoring system (GOOSS) after EUS-GE was 2.2. During a mean follow-up of 131 days, 10 patients (7.4%) need reintervention. Adverse events, including stent mal-displacement, bleeding and migration, occurred in 16 patients (13.1%). EUS-GE is an emerging and minimally invasive procedure that has efficacy and safety comparable with those of current therapies for the management of malignant GOO.

Curriculum Vitae

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Dr. Yu-Ting Kuo is attending physician at the Division of Endoscopy of National Taiwan University Hospital. He graduated from the Medical school of Tzu-Chi University and got Master of Science degree in Epidemiology and Preventive Medicine (MSc) at National Taiwan University. He completed Internal Medicine and Gastroenterology training at the National Taiwan University Hospital. He was also a visiting staff of biliarypancreatic department at The University of Tokyo Hospital in 2014. His main interests are all kinds of therapeutic endoscopy, especially endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound (EUS)/Interventional EUS in hepatopancreato-biliary area.

He has been an instructor of EUS education programs in digestive endoscopy society of Taiwan (DEST) since 2016. In addition, he attended different Asia EUS Group (AEG) EUS training programs, including 2nd Prince of Wales Hospital AEG Train the Trainer (TTT) EUS Course in Hong Kong, in 2015, 3rd Focused Interventional Workshop on EUS-guided Drainage of Per-pancreatic Fluid Collections in Hong Kong, in 2015 and Asian EUS Summit 2016 - Interventional EUS in Seoul Korea, in 2016, respectively. He also completed the training program of 1st WEO International School of EUS (WISE) in 2018.

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2012-2016 Tokyo Medical University, Dept. of Gastroenterology and Hepatology, Medical Doctor
2016-2020 Tokyo Medical University, Dept. of Gastroenterology and Hepatology, Assistant Professor
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Japanese Society of Internal Medicine —Fellow
Japanese Society of Gastroenterology (JSGE) — Fellow
Japan Gastroenterological Endoscopy Society (JGES) —Fellow
Japan Biliary Association (JBA) —Fellow
Japan Pancreas Society (JPS) —Councilor
American Society Gastroenterological Endoscopy (ASGE) - International Membership

Public work (Members in Japan)
Committee member of Tokyo Guidelines for acute cholangitis and cholecystitis
Committee member of JPN Guidelines for the management of acute pancreatitis
Committee member of Guidelines for post ERCP pancreatitis
Committee member of Guidelines for walled-off necrosis
Current status and future perspectives of Interventional EUS in Asia focused on EUS-guided gallbladder drainage in South Korea

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Laparoscopic cholecystectomy is considered the standard and preferred treatment for acute cholecystitis (AC). However, this surgical option may not be suitable for certain patients who are not ideal candidates for surgery due to various factors. Recently, endoscopic ultrasound (EUS)-guided gallbladder (GB) drainage (EUS-GBD) represents a potentially disruptive technology, as it offers a less invasive alternative to traditional surgical approaches. As a result, therapeutic strategies are experiencing a notable paradigm shift, leaning towards minimally invasive treatments. While the field is continuously evolving, several devices and techniques are currently being developed to facilitate easier and safer procedures for EUS-GBD. Indeed, recent innovations in the field of EUS-GBD, such as the lumen-apposing metal stents (LAMSs) with bidirectional anchoring flanges, have significantly improved outcomes for patients requiring drainage. Additionally, the use of LAMS has proven to be not only safe and reliable for cases of acute cholecystitis but also beneficial in enhancing the quality of life for patients who may not be ideal candidates for surgical treatment.

As an endosonographer performing EUS-GBD, there are several questions and uncertainties surrounding this procedure. Some of the key questions include:

1. Optimal Patient Selection: What are the specific criteria for identifying the most suitable candidates for EUS-GBD? Which patients are likely to benefit the most from this procedure compared to other treatment options?
2. Long-term Management: What are the long-term outcomes and potential complications associated with EUS-GBD?
3. Stent Selection: What factors should be considered when selecting the appropriate stent for EUS-GBD?
4. Comparisons with Surgical Options: How do the outcomes of EUS-GBD compare to traditional surgical interventions, such as laparoscopic cholecystectomy, in terms of efficacy, safety, and patient satisfaction?
5. Timing of Intervention: In what situations is EUS-GBD best utilized as a definitive treatment, and when is it more appropriate as a bridging therapy until surgical options become feasible?
6. Complication Management: How should potential complications, such as bile reflux, stent migration, or food impaction, be managed in patients undergoing EUS-GBD?
7. Future Developments: What ongoing research and technological advancements are being pursued to further improve the efficacy, safety, and overall outcomes of EUS-GBD?

Addressing these questions through further research, collaboration among endosonographers, and shared experiences will contribute to a deeper understanding and optimization of EUS-GBD as a valuable therapeutic option for patients.
Radiofrequency ablation: A novel endoscopic focal treatment of pancreatic cancer

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Pancreatic ductal adenocarcinoma (PDAC) is a leading cause of cancer death worldwide. Surgery is the only possible complete treatment for these patients. However, there is no effective screening tool, and patients often present with nonspecific symptoms, resulting in early diagnosis of resectable disease in only 10-15% of cases. The lack of new systemic treatment agents and an immunosuppressive tumor microenvironment have resulted in a persistently low 5-year survival rate of around 10% for pancreatic adenocarcinoma, which is far behind other malignant diseases. In the near future, pancreatic cancer is expected to become the leading cause of cancer-related mortality.

Several attempts, such as neoadjuvant chemotherapy and radiation therapy, have been applied in the treatment of pancreatic adenocarcinoma for decades. However, these approaches have only resulted in a dismal improvement in survival.

Radiofrequency ablation (RFA) is a thermal ablation technique that has been used for a long time in the treatment of liver and thyroid tumors. It employs an alternating RF current to generate heat and induce coagulation inside the tumor. RFA has been reported to induce an antigen-presenting effect and amplify weak tumor-related immunity which is crucial in cancer treatment. In addition, the technical success rate and procedure-related complication rate are acceptable, with complications usually being manageable non-surgically according to literature reviews. Although the overall survival benefit of combining RFA with PDAC treatment remains controversial, several existing studies have revealed better outcomes when RFA is combined with neoadjuvant chemotherapy.

In this retrospective single-center experience review, RFA was found to enhance treatment response in some patients, while others did not benefit. Further investigation into the potential benefits of RFA for patients is essential.
Liver

Tailoring multiple lines of systemic therapy for advanced HCC

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Speaker (J): JKT4-1
Tailoring systemic treatment based on tumor burden for advanced hepatocellular carcinoma.
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Speaker (K): JKT4-2
Surgical Conversion in Locally Advanced Hepatocellular Carcinoma Through Multimodal Systemic Therapy
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Speaker (T): JKT4-3
Proton Therapy for Hepatocellular Carcinoma
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Rising Star Program (J): JKT4-1-RS1
Importance of preclinical rationales to establish appropriate treatment sequences in the era of chemo-diversity for HCC
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Role of liver-directed therapy for advanced hepatocellular carcinoma in the era of combination immunotherapy
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Tailoring systemic treatment based on tumor burden for advanced hepatocellular carcinoma.

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The systemic therapy for advanced hepatocellular carcinoma (HCC) has shifted from molecular target agents to immunotherapy. Globally, six immunotherapies, including atezolizumab + bevacizumab, STRIDE (tremelimunab + durvalumab), atezolizumab + cabozantinib, durvalumab monotherapy, tislelizumab, and pembrolizumab, have shown positive results in clinical trials. In Japan, three immunotherapies, including atezolizumab + bevacizumab, STRIDE, and durvalumab monotherapy, as well as five molecular target agents (sorafenib, lenvatinib, regorafenib, cabozantinib, and ramucirumab), can be used as systemic treatments for unresectable HCC. Following the insurance coverage of STRIDE and durvalumab, the Japanese guidelines for hepatocellular carcinoma treatment were revised. STRIDE is recommended as one of the first-line treatments, and durvalumab is recommended as one of the treatments when combination immunotherapies are not suitable. The treatment algorithm for systemic therapy in the guidelines was also revised. After the approval of atezolizumab + bevacizumab, the first-line systemic therapy shifted from lenvatinib to atezolizumab + bevacizumab, and most of the second-line treatment after atezolizumab + bevacizumab was lenvatinib, based on the results of the HERITAGE study, which analyzed real-world data of systemic therapy for hepatocellular carcinoma in Japan. In real practical settings in Japan, STRIDE is used as the second-line systemic therapy after atezolizumab + bevacizumab. However, the efficacy and safety of STRIDE after atezolizumab + bevacizumab remain unclear. The emergence of these immunotherapies has changed the treatment target to the objective response rate (ORR) because the ORR correlates with overall survival. Several ongoing clinical trials in Japan aim to achieve a higher ORR. One of the treatments is lenvatinib combined with intrahepatic arterial infusion of cisplatin (LEN + CDDP), which has shown an ORR of more than 50%. The ORR of Atezolizumab + bevacizumab and STRIDE is 30% and 20%, respectively. Meanwhile, STRIDE showed a higher rate of progressive disease (PD) although it showed longer durable response. Considering these ORRs and the PD rate, one idea is tailoring systemic treatment based on tumor burden. STRIDE can be selected as the first-line treatment in cases of low tumor burden, and LEN + CDDP can be selected in cases of high tumor burden. Comprehensive genome profiling (CGP) was approved in Japan for second or later treatment selection. We have experienced some cases where treatment was selected based on CGP.
Surgical Conversion in Locally Advanced Hepatocellular Carcinoma Through Multimodal Systemic Therapy

Su Jong Yu
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In recent years, advanced Hepatocellular Carcinoma (HCC) management has seen remarkable advancements. The combination of atezolizumab and bevacizumab in immunotherapy achieved a groundbreaking 12% Complete Response (CR) rate, potentially transforming the treatment landscape for previously deemed incurable HCC(1). Even in cases where programmed cell death protein-1/programmed cell death ligand-1 antibody therapy had failed, promising outcomes were observed with lenvatinib monotherapy(2).

However, a significant challenge arises when patients achieve radiologically favorable responses through multimodal systemic therapy. The optimal course of action becomes uncertain—should they undergo aggressive interventions like surgery or transplantation, continue with maintenance therapy, or simply be closely monitored? Research led by Mazzaferro has shed light on this complex dilemma(3). Liver transplantation emerged as a significant contributor to improved survival, with a median Overall Survival (mOS) of 14.5 months. Notably, an important distinction emerged: patients achieving a partial response after downstaging and conversion experienced a substantially prolonged mOS of 28.3 months, whereas those with CR who did not proceed to transplantation had a lower mOS of 9.9 months. This underscores that radiologically favorable responses may not consistently align with pathologically favorable responses, and some patients with radiologically favorable responses may still face disease progression, often due to refusals to re-transplantation.

Furthermore, other studies have underscored that some patients who initially respond to treatment may eventually experience disease progression(4). This underscores the significance of considering curative options such as conversion surgery or local ablation for individuals achieving radiologically favorable responses through immunotherapy, potentially extending their survival(5).

On a different front, research has illuminated the possibility of surgical conversion in initially unresectable HCC through systemic or local therapies. Previous attempts with two-drug combinations yielded discouraging conversion rates, typically around 15-20%(6). Current studies are focused on comprehensive combination therapies that merge hepatic arterial infusion chemotherapy (HAIC)-based locoregional therapy with targeted therapy and immunotherapy(7). This innovative approach aims to bolster surgical conversion rates and achieve more favorable objective responses by harnessing synergistic effects.

While data on combination immunotherapy for downstaging and conversion to surgery remain limited and require further research, these breakthroughs herald a new era in HCC treatment. They offer fresh opportunities and improved outcomes for patients with advanced disease, holding the promise of a brighter future for individuals who were once considered untreatable.

References

Curriculum Vitae

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Educational Background
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3. Doctor of Philosophy in Medical Science, Graduate School, Seoul National University (March 1, 2010 - February 24, 2012)

Professional Experience
1) Clinical Professor, Department of Internal Medicine & Liver Research Institute, SNU College of Medicine (2011.03 ~ Present)
2) Visiting Scientist, NCI, NIH (Bethesda, MD, USA) (2016 ~ 2018)
3) Seoul National University College of Medicine, Doctor of Medicine (2010 ~ 2012)
4) Seoul National University College of Medicine, Master of Medicine (2004 ~ 2006)
5) Seoul National University College of Medicine, Bachelor of Medicine (1997 ~ 2001)

Other Experience and Professional Memberships
1) Academy Affairs Director, KLCA (2022.07 ~ Present)
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Proton Therapy for Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) is one of the most common cancers in the world. Most HCC patients have impaired liver function because of hepatitis or liver cirrhosis, and only approximately 20-40% of patients are candidates for resection. Maximal preservation of normal liver volume and function is an important consideration in the choice of treatment.

Proton beam therapy (PBT) for HCC treatment has been applied for decades, and many clinical results have shown excellent 3-year to 5-year local control (LC) rate ranging from 85-95% and nearly no major complications.

From 2015 to 2023, more than 6000 patients were treated with PBT at Chang-Gung Memorial Hospital. More than a quarter of patients have liver cancers. The PBT was considered in the patients that were not suitable for surgery or radiofrequency (RFA) and discussed in the multidisciplinary conference. The PBT dose were 72.6CGE/22fx and 66CGE/10fx, depending on tumor location. The largest tumor diameter was more than 5 cm, and more than 30% of tumors are larger than 10 cm in diameter. More than 40% were major tumor vascular invasion. The in-field control rate was more than 90%.

According to previous clinical results and our experiences, PBT can be a good alternative treatment for patients unsuitable for surgery.

Curriculum Vitae

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Importance of preclinical rationales to establish appropriate treatment sequences in the era of chemo-diversity for HCC

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Introduction
Nowadays, we have multiple lines of systemic therapy for hepatocellular carcinoma (HCC). We also have multiple conventional locoregional treatments. In the era of chemo-diversity, we face a new unmet medical need of difficulty in tailoring appropriate treatment sequences. In this point of view, the balance between preclinical rationale and clinical relevance is important to find appropriate treatment sequences. The purpose of this study is to accumulate preclinical rationales to establish appropriate treatment sequences by clarifying the change of tumor immune microenvironment (TIME) and molecular patterns in approved molecular targeted agents (MTAs) and locoregional treatment, hepatic arterial infusion chemotherapy (HAIC) using cisplatin and 5-fluorouracil.

Methods
We established immune syngeneic orthotopic HCC mouse models and treated them with each approved MTA (sorafenib, lenvatinib, regorafenib, ramucirumab, and cabozantinib) to evaluate the change of TIME in each drug. We also compared the therapeutic effects of atezolizumab plus bevacizumab (AB) with and without the pretreatment of HAIC. Moreover, we evaluated the influence of HAIC on HCC using the resected specimens in clinical samples.

Results
All MTAs commonly reduced infiltration of regulatory T cells and macrophages, which suggested that these changes were induced by the inhibition of VEGF signaling. Cabozantinib particularly induced the infiltration of dendritic cells, and lenvatinib significantly increased the infiltration of cytotoxic T cells and granzyme B-positive cells, which suggested that TIME has altered to a "hot" environment. To clarify why lenvatinib altered the TIME to "hot", experiments using a pan-FGF receptor inhibitor were conducted. The FGF receptor inhibitor also increased the infiltration of cytotoxic T cells and granzyme B-positive cells. Taken together, these results suggest that inhibition of the FGF signal is important to the alteration of TIME to "hot". The therapeutic response (objective response rate: with or w/o pretreatment HAIC; 60.8% v.s. 29.7%, p<0.001), progression-free survival (median; 5.5 months v.s., 5.2 months, p<0.05), and overall survival (median; 12.7 months v.s. 9.9 months, p<0.05) of patients treated with AB were superior in the pretreatment HAIC group. The expression of PD-L1 was significantly increased in HCC specimens treated with HAIC before hepatic resection. Cisplatin and 5-fluorouracil directly induced the expression of PD-L1 in human hepatoma cell lines.

Conclusions
Lenvatinib had promising effects to alter TIME to an immune "hot" environment and HAIC might have another role as a neo-adjuvant treatment to enhance the therapeutic effects of treatments using immune checkpoint inhibitors. Accumulation of preclinical rationales leads to establishing appropriate sequential treatments in the era of chemo-diversity for HCC.

Curriculum Vitae

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Peer-reviewed articles: Total 106 (first or corresponding author: 24)
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Tailoring multiple lines of systemic therapy for advanced HCC

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The management of hepatocellular carcinoma (HCC) has been transformed by the emergence of multi-targeted kinase inhibitors (TKIs) and immune checkpoint inhibitors (ICI). Recently conducted phase III trials have shown that combination therapy, which includes ICI, has surpassed sorafenib as the primary treatment choice for advanced HCC. This shift is due to the higher response rate and improved survival benefits offered by combination therapy. Currently, as the first line treatment for the advanced HCC patients atezolizumab and bevacizumab combinations or tremelimumab and durvalumab combination are recommended. For those who are not feasible to those immune check inhibitor combinations, such as underlying moderate to severe autoimmune disease or HCC recurrence after liver transplantation, TKIs such as lenvatinib or sorafenib are recommended as alternative first line options. So far, there is only evidence for second line treatment after sorafenib treatment including regorafenib, nivolumab plus ipilimumab, or pembrolizumab. The development of multiple lines of systemic therapy might lead to improving overall survival and quality of life for patients with advanced HCC. However, determining the optimal sequencing and tailoring of these therapies remains a complex task due to the heterogeneity of the disease and the limited understanding of individual patient characteristics that drive treatment responses. Examining a comprehensive set of clinical, molecular, and genetic factors might be needed to identify predictive biomarkers and treatment response indicators that can guide personalized therapeutic approaches. These approaches will provide insights into the evolving landscape of HCC treatment and contribute to the development of evidence-based guidelines for tailoring therapy in advanced HCC, which might shed light on the potential of targeted therapies, immunotherapies, and combination regimens in the management of advanced HCC.

Curriculum Vitae

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RECENT PUBLICATIONS
Role of liver-directed therapy for advanced hepatocellular carcinoma in the era of combination immunotherapy

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Surgery remains the primary method for curing hepatocellular carcinoma (HCC), although determining resectability is a complex issue that depends on tumor factors and the remnant liver function. It is estimated that approximately 60-70% of HCC cases are considered unresectable at the time of diagnosis. In unresectable HCC, systemic therapies such as multikinase inhibitors and immune checkpoint inhibitors (ICIs) are currently the standard treatment, but they primarily provide disease control rather than a cure.

Liver-directed therapy (LDT) can offer potential benefits to patients with advanced HCC in various scenarios. Firstly, the combination of LDT with ICIs may lead to a synergistic effect through the stimulation of systemic immune response by releasing neoantigens into the bloodstream and augmenting the proliferation of tumor-specific T cells. Several pilot studies had demonstrated promising results using the combination of ICIs and LDT, including ablation, Y90-radioembolization, hepatic arterial infusion chemotherapy, transarterial chemoembolization and stereotactic body radiation therapy in unresectable HCC.

Combination immunotherapy has shown promising results with higher objective response rates, including anti-VEGF plus ICIs, multikinase inhibitors plus ICIs, or dual ICIs. Following the successful combination ICI treatment, which results in significant tumor shrinkage, applying LDT to the remaining lesion offers the opportunity for cure even in advanced HCC cases.

As combination ICIs have resulted in significantly higher tumor responses, several studies have investigated their application in the neoadjuvant setting, and the results are very promising. Of note, a proportion of patients achieved complete pathological responses after neoadjuvant ICIs, which raises a new question regarding the necessity of adding LDT in such exceptional responders.

In summary, current evidence highlights the importance of combination immunotherapy and LDT in improving treatment outcomes and potentially offering a chance of cure for advanced HCC patients.

Curriculum Vitae

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Dr. Su completed his medical education at the School of Medicine, Kaohsiung Medical University, in 2012. He subsequently obtained board certifications in internal medicine in 2017 and oncology in 2019. Currently, Dr. Su holds the position of Assistant Investigator at the National Health Research Institutes and serves as a visiting staff physician at the Department of Oncology in the National Cheng Kung University Hospital.

Dr. Su’s primary research focus lies in the field of clinical and translational research pertaining to the development of new drugs and clinical trials for hepatobiliary and pancreatic cancers. Additionally, he actively participates in real-world data manipulation and employs next-generation sequencing techniques, such as whole exome sequencing, cell-free DNA analysis, whole transcriptome sequencing, single-cell RNA sequencing, and metagenomics. In recognition of his research contributions, Dr. Su has been honored with prestigious awards, including the Japanese Society of Medical Oncology (JSMO) Young Investigator Award in 2022 and 2023, the JSMO-Rising Stars in Asia workshop Award in 2023, and the Taiwan Joint Cancer Conference (TJCC) Best Poster Award in 2022 and 2023.

Dr. Su takes on additional roles within the medical community, serving as the executive secretary of the Taiwan Liver Cancer Association (TLCA) Research Group, the chief staff of the core measure development committees for pancreatic cancer under the Ministry of Health and Welfare in Taiwan, and the executive secretary of the consensus development committees in pancreatic cancer within the Taiwan Pancreas Society. Throughout his career, Dr. Su has published over 20 articles in esteemed peer-reviewed journals, including the International Journal of Surgery, Gastrointestinal Endoscopy, and the British Journal of Cancer.