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EDITORIAL

ON THE OCCASION OF WORLD CANCER DAY – 4TH FEBRUARY
PEOPLE WHO CREATED HISTORY – MARIE CURIE

Marie Skłodowska Curie (7th November 1867 – 4th July 1934) was a Polish and naturalized-French physicist and chemist who conducted pioneering research on radioactivity. She was the first woman to win a Nobel Prize, the first person and only woman to win twice, the only person to win a Nobel Prize in two different sciences, and was part of the Curie family legacy of five Nobel Prizes.

Maria was born in Warsaw. In her early childhood the family had lost their property and fortunes through patriotic involvements in Polish national uprisings aimed at restoring Poland's independence. This condemned the subsequent generation, including Maria and her elder siblings, to a difficult struggle to get ahead in life. Maria's mother operated a prestigious Warsaw boarding school for girls; she resigned from the position after Maria was born. She died of tuberculosis in May 1878, when Maria was ten years old. Less than three years earlier, Maria's eldest sibling, Zofia, had died of typhus. In 1891, aged 24, she followed her elder sister to study in Paris, where she earned her higher degrees and conducted her subsequent scientific work. She subsisted on her meager resources, keeping herself warm during cold winters by wearing all the clothes she had. She focused so hard on her studies that she sometimes forgot to eat. Skłodowska studied during the day and tutored evenings, barely earning her keep.

Skłodowska began her scientific career in Paris with an investigation of the magnetic properties of various steels, when Pierre Curie entered her life; it was their mutual interest in natural sciences that drew them together. Eventually Pierre Curie proposed marriage, but at first Skłodowska did not accept as she was still planning to go back to her native country. Curie, however, declared that he was ready to move with her to Poland, even if it meant being reduced to teaching French. On 26 July 1895 they were married in Sceaux. In 1897, her daughter Irène was born. To support her family, Curie began teaching. The Curies did not have a dedicated laboratory; most of their research was carried out in a converted shed next to the School of Physics and Chemistry. The shed, formerly a medical school dissecting room, was poorly ventilated and not even waterproof. They were unaware of the deleterious effects of radiation exposure.

Curie's systematic studies included two uranium minerals, pitchblende and torbernite (also known as chalcolite). By 1898 she discovered that the element thorium was also radioactive. Pierre Curie was increasingly intrigued by her work. By mid-1898 he was so interested in it that he decided to drop his work on crystals and join her. She was acutely aware of the importance of promptly publishing her discoveries and thus establishing her priority. In July 1898, Curie and her husband published a joint paper announcing the existence of an element which they named "polonium", in honour of her native Poland. On 26 December 1898, the Curies announced the existence of a second element, which they named "radium", from the Latin word for "ray". In the course of their research, they also coined the word "radioactivity".Between 1898 and 1902, the Curies published, jointly or separately, a total of 32 scientific papers, including one that announced that, when exposed to radium, diseased, tumor-forming cells were destroyed faster than healthy cells.In june 1903 the couple was invited to the Royal Institution in London to give a speech on radioactivity; being a woman, she was prevented from speaking, and Pierre Curie alone was allowed to. The Curies did not patent their discovery and benefited little from this increasingly profitable business.

Curie and her husband declined to go to Stockholm to receive the Nobel prize in person; they were too busy with their work, and Pierre Curie disliked public ceremonies. As Nobel laureates were required to deliver a lecture, the Curies finally undertook the trip in 1905. The award money allowed the Curies to hire their first laboratory assistant. Following the award of the Nobel Prize, the University of Paris gave him a professorship and the chair of physics. In December 1904, Marie Curie gave birth to her second daughter, Ève. On 19 April 1906, Pierre Curie was killed in a road accident. he was struck by a horse-drawn vehicle and fell under its wheels, causing his skull to fracture. Curie was devastated by her husband's death.On 13 May 1906 the physics department of the University of Paris decided to retain the chair that had been created for her late husband and to offer it to Marie. She accepted it, hoping to create a world-class laboratory as a tribute to her husband Pierre. She was the first woman to become a professor at the University of Paris.International recognition for her work had been growing to new heights, and the Royal Swedish Academy of Sciences honored her a second time, with the 1911 Nobel Prize in Chemistry. Curie's second Nobel Prize enabled her to persuade the French government into supporting the Radium Institute, built in 1914, where

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VASCULAR RESECTION IN PANCREATIC CANCER

Introduction

Pancreatic ductal adenocarcinoma (PDAC) is associated with a poor prognosis, with only 5 % of patients surviving 5 years after the diagnosis. Surgical resection remains the only available curative therapy. However, only10–20% of patients are candidates for resection as approximately 50% present with metastases and 35 % with locally advanced or unresectable disease at time of diagnosis. Traditionally, the standard approach for potentially resectable disease has been surgery followed by adjuvant therapy. With the recent adoption of multimodal treatment strategy for PDAC, concomitant major vessel resection and reconstruction have been aggressively done, leading to comparatively better pathologically negative surgical margins and postoperative survival. This review gives an overview of the current status of vascular resection in management of PDAC.

Evaluation for vascular resection

High-quality computed tomography (CT) scan is the standard of care for determining resctability of primary tumor. With the recent advances in imaging techniques, a new group of patients known as borderline resectable PDAC, previously considered poor candidates for resection because of the relationship of their primary tumor to surrounding vasculature, has been defined. The International Study Group for Pancreatic Surgery (ISGPS) has published a consensus statement to define borderline resectable diseases in accordance with the guidelines of the National Comprehensive Cancer Network (NCCN). Three grades of resectability were defined for PDAC as resectable, borderline resectable and unresectable.

PDAC is defined as resectable if tumor extension to the celiac and superior mesenteric artery (SMA) is absent, the superior mesenteric vein (SMV) and portal vein (PV) are patent, and there are no distant metastases. Patients with focal tumor abutment (<180°) of the SMA, encasement of the gastroduodenal artery up to the hepatic artery, or involvement of the SMV/PV that is potentially resectable and reconstructable are considered borderline resectable. Unresectability is defined as an encasement (more than one half of the vessel circumference) or occlusion/ thrombus of the SMA, unreconstructable SMV or SMV-PV confluence occlusion, or direct involvement of the inferior vena cava, aorta, or celiac axis. The rationale for combining vascular resection with pancreatectomy is to increase the probability of achieving a R0 resection.

NCCN guidelines for pancreatic cancer version 1.2019

Patients categorized as borderline resectable on the basis of venous or arterial involvement are usually given some form of neodjuvant therapy (chemotherapy or chemoradiotherapy) after inter disciplinary board discussion and as per institutional protocol. As current imaging cannot distinguish between cancer induced desmoplasia or radiotherapy / chemotherapy induced fibrosis or fibrosis due to tumor regression, a surgical exploration is recommended in patients with tumor regression as well as in patients with a stable disease after neoadjuvant therapy. Patients with a clear tumor progression after neoadjuvant treatment should be planned for palliative care only.

Venous resection

Historically, major vessel involvement was a contraindication to resection in patients with PDAC. In 1973, Fortner described a surgical approach of regional pancreatectomy involving en bloc resection of peripancreatic soft tissue, regional lymph nodes with resection of the PV (type I),or resection and reconstruction of a major artery (type II). Although these extended resections achieved improved resectability rates they were associated high morbidity (67 %) and mortality (23 %). These results discouraged generalized adoption of major vessel resection and reconstruction. However with recent advances in surgical and anaesthesia techniques reduction in surgical morbidity and mortality could be achieved. In contrast to arterial resection, pancreatoduodenectomy (PD) with PV resection have gained widespread acceptance in centers around the world and can be performed safely with no increase in perioperative morbidity or mortality compared to standard PD.

When the PV or SMV is involved, venous excision is done either by a segmental resection or by a tangential resection. In case of segmental resection, the reconstruction requires an end-to-end anastomosis either by direct anastomosis or by using an interposition venous or prosthetic graft. For this purpose, autologous grafting (e.g., renal vein, internal jugular vein) is possible but requires venous harvesting before clamping and resection. Alternatively, synthetic grafts, i.e., ringed goretex prosthesis, can be chosen to bridge the resected vein segment. Wide resection of the PV may require transection of the splenic vein. To avoid segmental portal hypertension, end-to-side reanastomosis of the splenic vein to the interposition graft is recommended.

It has been shown in various studies that both the resection with a direct anastomosis and the interposition of a graft can be performed safely. Numerous authors have reported a mortality rate below 5 % in patients undergoing venous resection with PD, similar to that of standard PD. Siriwardana et al reported a systematic review on the outcome of synchronous PV-SMV resection during pancreatectomy for cancer. Their analysis included a total of 52 studies and 1646 patients undergoing vein resection with PD. The median morbidity rate was 42 %, and the mortality rate was 5.9 %. The reported long-term survival in the review for 1351 patients was 13 months, with 1-, 3-, and 5-year overall survival rates of 50, 18, and 8 %, respectively.

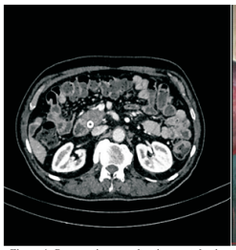

Figure 1: Pancreatic mass abutting portal vein

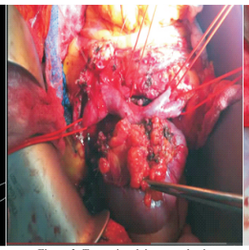

Figure 2: Tumor involving portal vein

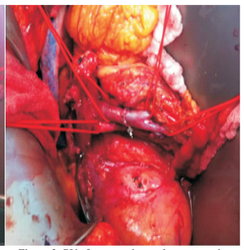

Figure 3: PV after resection and anastomosis

Another recent meta-analysis by Zhou et al, involved 19 studies of pancreatectomies for pancreatic cancer and included 661 patients with and 2247 patients without portomesenteric venous resections. Surgical outcomes were comparable in both groups. They found no difference in the overall survival between the cohorts and a 5-year survival rate of 12.3 %, certainly superior to palliative treatment. With favorable morbidity and mortality, long-term survival after these resections are much better compared to patients with only palliative management. Therefore, resection of the PV and SMV can be regarded as a standard procedure in experienced hands and should be performed routinely to achieve R0 resection.

Arterial resection

Arterial resection for PDAC has remained an area of controversy since Fortner first introduced the concept as part of regional pancreatectomy. Many authors regard the invasion of hepatic artery, the celiac axis or SMA, as a contraindication to surgery, because of the high morbidity and mortality rates associated with arterial resection and reconstruction.

Although limited arterial invasion is considered as borderline resectable according to the ISGPS consensus statement, an upfront resection is rarely recommended, even if it can technically be performed. Recently, with the advent of more effective systemic therapies, few authors have investigated the potential benefit of removing the primary tumor, even in the setting of complex arterial abutment or encasement, when it is the only site of disease after neoadjuvant therapy. After re-staging, patients are subjected to surgical exploration as long as no signs of systemic tumor spread are present. Using this approach, in 33–50 % of all primarily unresectable patients, a radical resection is possible which achieves R0 resection rates comparable to standard resection.

In a meta-analysis of 26 studies, Mollberg et al compared 366 patients undergoing arterial resection and 2243 patients without arterial resection. Perioperative morbidity (median 53.6 %) and mortality (median11.8%) were significantly higher in arterial resection group. Survival analysis did not show a benefit compared with patients who underwent only venous resection. However when compared with patients who did not undergo resection, the1-year survival was favorable being threefold greater for patients with arterial resection.

Regarding resection of the SMA, only few studies are available including a total number of less than 30 patients. All of them showed that the resection is technically possible and grafting with the saphenous vein was the most commonly used method for reconstruction. But morbidity of this approach is high and the oncological outcomes are not yet convincing to recommend it as a routine practice. Celiac axis or hepatic artery resection is performed more commonly. Current literature includes approximately 200 patients on this topic. Surgical morbidity is up to 40 %, and ranges from 0 to 35 %, showing the inconsistency of data for this approach. In summary, arterial resection can be carried out safely in experienced hands, but currently it is not recommended as standard of care.

Conclusion

Radical R0 resection is the standard curative treatment of PDAC. Venous resection with pancreatic resection meets this Oncological requirement without increasing the morbidity and mortality. Therefore, major venous involvement should not be considered a contraindication to resection of borderline resectable PDAC. Arterial resection is not recommended as a routine practice at present. All patients must be managed by multimodality approach as radical resection alone cannot achieve optimal patient outcome.

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Fellow - Surgical Oncology

Dr. Shivendra Singh
Sr. Consultant & Chief of GI & HPB Oncosurgery

From the Desk of the

Medical Director

Rajiv Gandhi Cancer Institute and Research Centre, Niti Bagh

The Niti Bagh Centre of RGCIRC proudly enters its third year carrying with it the Institute's unique legacy of state of the art quality patient care within easy reach of all. Located in the heart of South Delhi, it offers full-fledged Medical and Surgical Oncology services along with a whole spectrum of Super - speciality Oncology clinics with the top experts in the field. Close collaboration and teamwork between the various disciplines is one of our unique strengths enabling us to provide patients with the best care available. Well known for its premier status as Asia's exclusive cancer centre, we at RGCIRC remain committed to Community Outreach programs offering an array of activities designed to educate patients, their families, care givers and the community about cancer related topics.

We hope to add a new 100 - bedded wing at Niti Bagh in the near future with state of the art Diagnostics, Operation Theatres and Radiotherapy facilities.

Watch this space for interesting case discussions.

Dr. Gauri Kapoor
MD, PhD

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research was conducted in chemistry, physics, and medicine. She was appointed Director of the Curie Laboratory in the Radium Institute. Led by Curie, the Institute produced four more Nobel Prize winners, including her daughter Irène Joliot-Curie and her son-in-law, Frédéric Joliot-Curie. In 1921, U.S. President Warren G. Harding received her at the White House to present her with the 1 gram of radium collected in the United States. In 1922 she became a fellow of the French Academy of Medicine.

Curie visited Poland for the last time in early 1934. A few months later, on 4 July 1934, she died at the Sancellemoz sanatorium in Passy, Haute-Savoie, from aplastic anemia believed to have been contracted from her long-term exposure to radiation. In her last year, she worked on a book, Radioactivity, which was published posthumously in 1935. She and her husband often refused awards and medals. Seventy five years after her death, Poland and France declared 2011 the Year of Marie Curie, Google celebrated the anniversary of her birth with a special Google Doodle. In 2007, a metro station in Paris was renamed to honour both of the Curies. Polish nuclear research reactor Maria was named after her. The 7000 Curie asteroid was also named after her. ***She was known for her honesty and moderate life style. Albert Einstein reportedly remarked that she was probably the only person who could not be corrupted by fame.***

Dr. A. K. Dewan
Director - Surgical Oncology

CME ON PANCREATIC CANCER

Department of GI Oncosurgery, RGCIRC, Delhi organized a CME on Pancreatic Cancer on Sunday, 25th November 2018 at Hotel Crowne Plaza, Rohini, Delhi under guidance of Dr. Shivendra Singh, Sr. Consultant & Chief of GI Oncosurgery and Dr. Vineet Talwar, Director - Medical Oncology. It covered all aspects of pancreatic cancer with special focus on management of borderline resectable pancreatic cancers and neuroendocrine tumors of pancreas. Renowned international and national faculty with expertise in pancreatic cancer shared their experience and knowledge. International faculty included Prof. J Lee (Head, Department of Surgical Oncology), Prof. Harmeet Kaur (Department of Radiology) and Prof. Michael J Overman (Department of GI Medical Oncology) from MD Anderson Cancer Center, USA and Prof. Thilo Hackert (Head, Pancreatic Unit, Department of HPB surgery) from Heidelberg university, Germany. It was attended by more than two hundred delegates from all over the

Architect's Impression of RGCIRC (post expansion)

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