Saudi Oncology Society clinical management guideline series

Pancreatic cancer 2014

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A total of 195 case of pancreatic cancer have been diagnosed in the Kingdom of Saudi Arabia (KSA) in 2010 accounting for 2.5% of all cancers for that year.[1] The age standardized rate was 2.2/100,000 for males and 1.6/100,000 for females.

A committee of experts in the medical and surgical treatment of pancreatic cancer was established under the supervision of the Saudi Oncology Society (SOS).

The evidence adopted in these guidelines is rated at 3 levels: 1) Evidence level (EL)-1 (highest level) evidence from phase III randomized trials or meta-analyses; 2) EL-2 (intermediate-level) evidence from good phase II trials or phase III trials with limitations; and 3) EL-3 (low-level) from retrospective or observational data and/or expert opinion. This easy-to-follow grading system is convenient for the reader and allows accurate assessment of the applicability of the guidelines in individual patients.[2]

All pancreatic cancer cases are preferably seen or discussed in a multidisciplinary form.

1. **Pre-treatment evaluation**
    - 1.1 Clinical examination, including age, performance status (PS), and degree of weight loss
    - 1.2 Blood count, liver, and renal function
    - 1.3 Tumor marker: CA19.9 level
    - 1.4 Computed tomography (CT) scan of chest, abdomen, and pelvis (preferably triple phase, spiral)[5] (EL-1)
    - 1.5 Endoscopic ultrasound (EUS) (optional) ± fine-needle aspiration (EL-2)
    - 1.6 Endoscopic retrograde cholangio-pancreatography (ERCP) (EL-2)
    - 1.7 Positron emission tomography (PET) scan (optional) (EL-2)
    - 1.8 Laparoscopy in resectable cases (optional) (EL-2)

2. **Surgical pathology report requirement.** The following parameters should be mentioned in all surgical pathology reports of pancreatic cancer:
    - 2.1 Specimen type
    - 2.2 Tumor size
    - 2.3 Histologic grade: G
    - 2.4 Primary tumor extent of invasion: T

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2.5 Regional lymph node: N
- 2.5.1 Number of nodes recovered
- 2.5.2 Number of nodes involved

2.6 Metastasis: M
2.7 Margins: surgical clearance in mm
2.8 Whipple's resection
- 2.8.1. Superior mesenteric artery (SMA) margin
- 2.8.2. Post margin
- 2.8.3. Portal vein margin
- 2.8.4. Pancreatic neck margin
- 2.8.5. Enteric margin

2.9 Lymphatic invasion: L
2.10 Vascular invasion: V
2.11 Perineural invasion: P
2.12 Final stage: G, T, N, M, L, V, P

3. Staging classifications:
The American Joint Commission on Cancer (AJCC)- 2007 pathological staging system will be used.[3]

4. Treatment:

4.1 Assessment of resectability: Tumors will be considered
- 4.1.1 Resectable: if there are clear fat planes around celiac trunk and superior mesenteric artery (SMA), and have patent superior mesenteric vein (SMV) and portal vein
- 4.1.2 Unresectable: if there is invasion of celiac trunk and SMA or if there is an occlusion of SMV or portal vein. Invasion of the superior mesenteric or portal vein is no longer an absolute contraindication. These veins can be resected partially with as much as 50% narrowing of the lumen
- 4.1.3 Borderline resectable: those are defined as one in which there is high likelihood of an incomplete resection (R1 or R2)[4,5]

4.2 Management of resectable pancreatic cancer:
- 4.2.1 Laparotomy and pancreatico-duodenectomy.[6,7] This should only be performed in a tertiary care facility. Pre-operative biopsy is not required
- 4.2.2 Adjuvant chemotherapy for 6 months. This is offered to all patients with pathological stage: T1-T4, N0-N1, and R0-R1 resection. Treatment consists of single agent gemcitabine at a dose of 1000 mg/m^2 on days one, 8, and 15. Cycle repeated every 28 days, for a total of 6 cycles[8] (EL-1)
- 4.2.3 Post-operative radiation is a possible option for R1-R2 resection. Radiotherapy dose should be 45-54 Gy (1.8-2.0 Gy/day) (EL-2)

4.3 Management of borderline resectable pancreatic cancer: options include one of the following:
- 4.3.1 Planned upfront resection. Further therapy will depend on findings during surgery:
  - 4.3.1.1 If found resectable: perform pancreatico-doudenectomy followed by adjuvant chemotherapy (see Item 4.2.2) (EL-1)
  - 4.3.1.2 If found unresectable: perform biopsy, consider doing bypass surgery and celiac plexus block. Postoperatively, patients can be offered chemotherapy alone (see item 4.4.2) or chemoradiotherapy[11] (EL-2).

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4.3.1.2.1 Options of chemotherapy with concurrent radiotherapy include:
4.3.1.2.1.1 5-fluorouracil 500 mg/m^2 daily for 3 days cycle repeated after 4 weeks[12] (EL-2)
4.3.1.2.1.2 Capecitabine at a daily dose of 800 mg/m^2 BID for 5 days per week for the duration of irradiation[9] (EL-2)
4.3.1.2.1.3 Gemcitabine 300-600 mg/m^2 weekly during irradiation.
4.3.1.2.2 Radiotherapy dose should be 45-54 Gy (1.8-2.0 Gy/day) [10] (EL-2)

4.3.2 Planned for upfront neoadjuvant therapy. Patient should have confirmatory tissue biopsy followed by either palliative chemotherapy (EL-2) or chemoradiotherapy (EL-2) (see item 4.3.1.2.1 and 4.3.1.2.2). Patients with major response can be considered for re-exploration and possible resection.

4.4 Management of locally advanced, unresectable pancreatic cancer. Patients should have the following:
4.4.1 Tissue biopsy
4.4.2 Palliative chemotherapy with one of the following options:
4.4.2.1 Single agent gemcitabine: dose of 1000 mg/m^2 on days one, 8, 15. Cycle repeated every 28 days, until progression (EL-1)
4.4.2.2 Gemcitabine based combinations (gemcitabine + fluoropyrimidines or gemcitabine + cisplatin)[11] (EL-1)
4.4.2.3 FOLFORINOX combination chemotherapy[12] (combination of 5-fluorouracil, leucovorin, oxaliplatin and irinotecan) in patients with PS 0-1 by ECOG scale (EL-1)
4.4.3 Palliative chemoradiotherapy using gemcitabine 11 (see item 4.3.1.2.1.3)

4.5 Management of metastatic pancreatic cancer. Patients may be offered palliative chemotherapy. The choice depends on patient age, PS, and patient choice after an informed consent. Chemotherapy is given until disease progression or unacceptable toxicity. Those options include:
4.5.1 Single agent gemcitabine (EL-1)
4.5.2 Gemcitabine based combinations (gemcitabine + fluoropyrimidines[13] or gemcitabine + cisplatin[11] or gemcitabine + nab-paclitaxel[14]) (EL-1)
4.5.3 FOLFORINOX combination chemotherapy[12] in patients with PS 0-1 by Eastern Cooperative Oncology Group (ECOG) scale (EL-1)
4.5.4 Patients not fit for chemotherapy should be given best supportive care. This includes, but is not restricted to pain management (including nerve block of celiac plexus, stenting for biliary obstruction. and duodenal obstruction)

4.6 Management of locally recurrent disease: options include
4.6.1 Concurrent gemcitabine and radiotherapy. Radiotherapy dose should be 45-54 Gy (1.8-2.0 Gy/day)[9] (EL-1)
4.6.2 Palliative chemotherapy (see item 4.5) (EL-1)
4.6.3 Best supportive care for unfit patients (see item 4.5.4)

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