tion of pancreatic tumors across 22 studies was 94% (80). Importantly, it has a very high negative predictive value (81, 82). This is valuable for clinicians as it indicates that EUS can also exclude pancreatic cancer. In patients with PDAC it is frequently used as a complementary staging tool to evaluate regional lymph nodes, define the degree of tumor-vascular involvement, or secure a definitive cytologic or histologic diagnosis (77, 83).

EUS-guided fine-needle biopsy (preferred over fine-needle aspiration) is the most favorable modality for obtaining tissue specimens from the pancreas (Fig. 6). However, preoperative tissue diagnosis may not be needed in surgical candidates with potentially resectable pancreatic lesions that are highly suspected of malignancy. While a positive sample can confirm the diagnosis, benign findings don't exclude the presence of malignancy. Once PDAC is suspected on initial imaging, the next step is generally a staging evaluation to establish disease extent and resectability rather than biopsy. A preoperative biopsy may be recommended if a diagnosis of chronic or autoimmune pancreatitis is suspected and differential diagnosis yields difficulties.

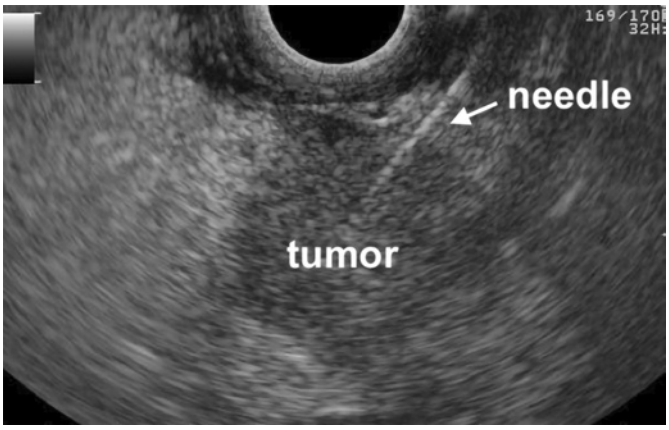
Therapy

Radical resection is the only potential curative approach in patients with PDAC. Neoadjuvant or adjuvant chemotherapy/chemoradiotherapy may improve disease-free survival and overall survival (OS) (84, 85). However, resection with curative intent is feasible only in 10%–20% of patients. Unfortunately, in these resected patients, positive resection margins are observed in the majority of cases. Thus, neoadjuvant chemotherapy or chemoradiotherapy is the standard of care in border-line resectable and locally advanced unresectable tumors. Chemotherapeutic intensive regimen with 5-fluorouracil, oxaliplatin, and irinotecan (FOLFIRINOX) results in a significantly better secondary resection rate and OS (85, 86).

In resectable PDAC, the current standard of care is resection followed by adjuvant chemotherapy or chemoradiotherapy. However, neoadjuvant therapy can be also considered in this setting, especially if risk factors are present, e.g., large primary tumors, enlarged lymph nodes, high baseline CA 19-9 levels, significant weight loss, or severe pain. Chemotherapeutic protocols for neoadjuvant and adjuvant treatment are interchangeable and are based on FOLFIRINOX regimen or gemcitabine/nab-paclitaxel combination (87).

Metastatic disease is an indication for palliative chemotherapy. This approach can prolong survival, decrease tumor-related symptoms, and preserve quality of life. For patients with a good performance status, intensive FOLFIRINOX regimen or gemcitabine/nab-paclitaxel combination are the standard of care, whereas gemcitabine or 5-fluorouracil alone are preferred for unfit patients (88).

Fig. 6. *Endoscopic ultrasound-guided fine-needle biopsy of a mass at the junction of the pancreatic head and body. Histopathologic findings confirmed the diagnosis of pancreatic ductal adenocarcinoma (PDAC)*



Currently, target therapy is still limited in PDAC and is feasible in only a minority of metastatic patients. Olaparib is a specific inhibitor of Poly (ADP-ribose) polymerase. In patients with germline *BRCA1* or *BRCA2* mutations who didn't progress on chemotherapy with platinum derivatives, olaparib results in a statistically-significant prolonged median progression-free survival (89). An immune checkpoint inhibitor pembrolizumab is already approved for patients who harbor high microsatellite instability, DNA mismatch repair deficiency, or high tumor mutational burden (90). NTRK inhibitors lacotrectinib and entrectinib may be considered among patients with PDAC harbouring NTRK fusion (87).

Conclusion

Pancreatic cancer remains one of the deadliest malignancies with dismal prognosis and limited options for effective therapy. It presents vaguely and heterogeneously, and the grim reality is that most patients have advanced or metastatic disease at diagnosis. In regards to the attempts at early detection of PDAC without the need for advanced or invasive methods, a discovery of a cost-effective biomarker with high specificity and sensitivity has currently been a goal of many researchers. Nonetheless, an effective screening tool is still not available. Contrast-enhanced CT using a dual phase pancreatic protocol remains the mainstay method for diagnosing PDAC and determining its resectability. EUS is an increasingly used adjunctive staging method that also allows for tissue diagnosis when necessary. Additionally, conscious indication of pancreatic imaging using MR may improve diagnostic rates in selected groups of patients.

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