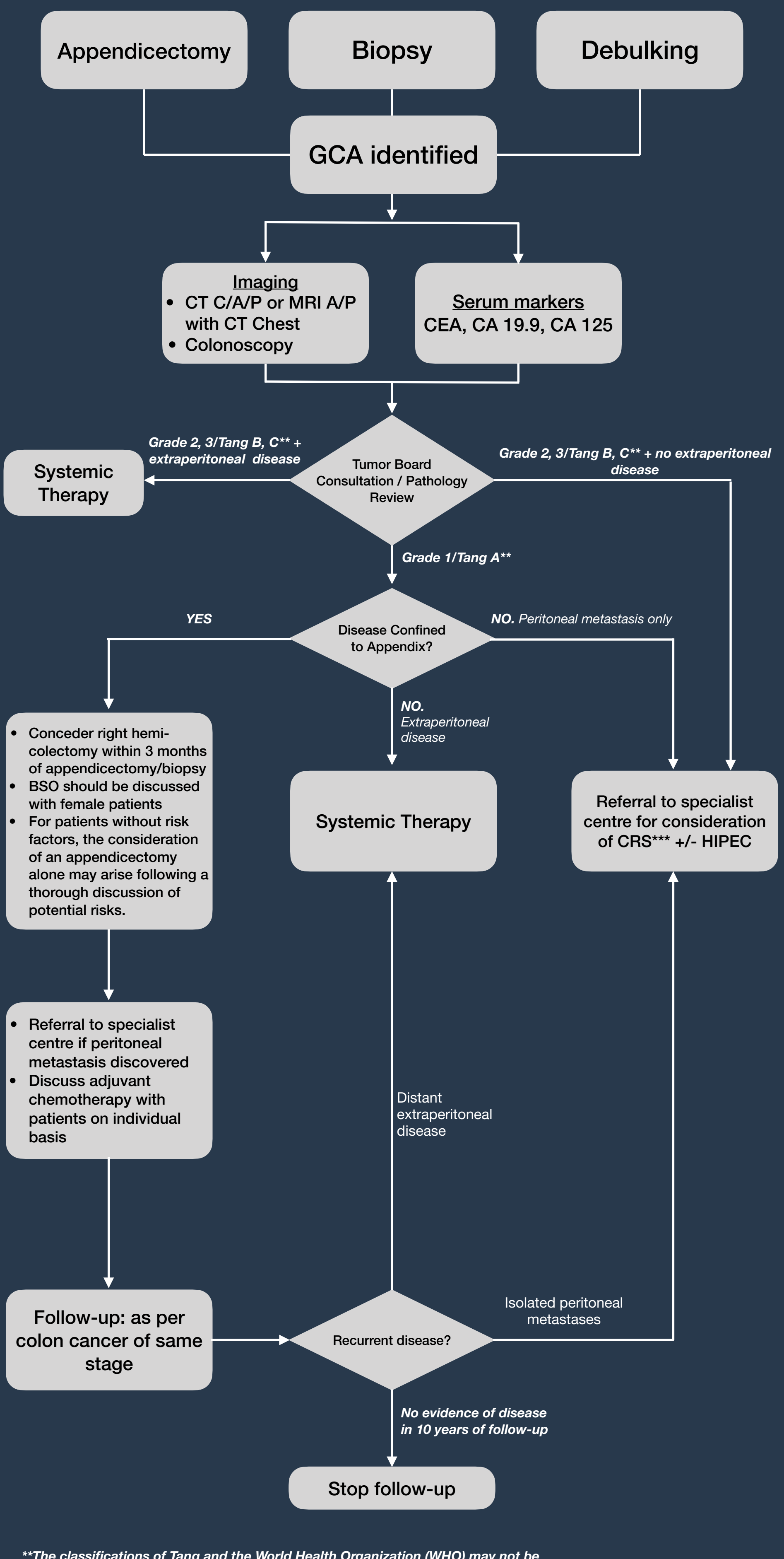
UKINETS Bitesize Guidance Goblet Cell Adenocarcinomas*

PAGE 1 - MANAGEMENT ALGORITHM



***The classifications of Tang and the World Health Organization (WHO) may not be interchangeable in all cases.*

**** Cytoredcutive surgery*

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PAGE 2 - NOTES

Goblet cell adenocarcinomas (GCAs), also known as Goblet cell carcinomas (GCCs) or previously referred to as goblet cell carcinoids, adenocarcinoids, or mucinous carcinoid appendix, exhibit characteristics that combine features of both adenocarcinomas and neuroendocrine tumors (NETs). Unlike NETs, GCAs are recognized for their heightened aggressiveness. Consequently, they are officially classified and staged as appendiceal carcinomas. It is crucial to underscore that GCA of the appendix should be regarded as a distinct pathological and prognostic entity when compared to pure neuroendocrine tumors of the appendix. The differentiation between these entities is pivotal for accurate diagnosis, treatment planning, and prognostic assessment.

GCAs of the appendix are very rare epithelial neoplasms: incidence 0.16/100 000 population/year [1].

Two thirds of cases are incidental findings after appendicectomy or ileo-caecal resection for abdominal pain and right iliac fossa mass.

Up to 40 percent of cases present with distant metastases to the peritoneum, liver, and/or ovaries [2] Consideration should be given to refer all patients diagnosed with GCAs to a specialist centre (NET/ Colorectal) for MDT review of diagnosis and treatment plan development.

Diagnostic workup:

CT scan of the thorax, abdomen and pelvis to look for metastasis. Alternatively, MRI of abdomen and pelvis can be performed.

Somatostatin receptor imaging (SRI) is very rarely positive and should not be done routinely. FDG PET may be useful in detecting disseminated disease in high grade tumours.

Tumour markers; CEA, CA 19-9 and CA 125 are more likely to be positive than neuroendocrine markers. Routine measurement of chromogranin A is not recommended.

Pathological review: Reporting should be according to RCPath dataset guidelines. The WHO (G1, G2, G3) and Tang (groups A, B, C) grading systems are associated with prognosis. [3, 4] Although they are not directly comparable, both systems have been included in the algorithm. Staging is according to UICC/AJCC as for adenocarcinoma of the appendix. Review of histology by a specialist GI or neuroendocrine histopathologist is recommended.

Treatment:

After undergoing an appendicectomy, it is recommended to consider a completion right hemicolectomy within three months of the initial surgery. However, the existing evidence regarding its benefits in terms of relapse-free and overall survival is limited, especially for small (T1/2 N0) and low-grade (Tang A) tumors. This approach should be personalized and discussed individually with patients.

Due to the risk of peritoneal spread to the ovaries, some suggest that prophylactic bilateral salpingo-oophorectomy may enhance relapse-free survival. Nevertheless, the evidence supporting this is insufficient, and decisions should be made on a case-by-case basis through discussion with patients.

For certain patients, cytoreductive surgery +/- hyperthermic intra-peritoneal chemotherapy (HIPEC) should be considered on an individual basis [5,6]. Referral to national peritoneal cancer services (e.g. Basingstoke, Manchester) for Multidisciplinary Team (MDT) review or advice is recommended. This is especially relevant for incompletely resected GCAs with stage II/III/IV [5] or patients with Tang B and C who require a right hemicolectomy, as they have a high risk of peritoneal spread observed intraoperatively and may benefit from CRS/HIPEC [6].

In terms of chemotherapy, adjuvant chemotherapy, while not evidence-based, can be considered in cases with a high risk of relapse, such as GCAs Tang B/C and/or stage II/III/IV. This consideration is particularly relevant after cytoreductive surgery +/- HIPEC in stage III/IV cases [3,7,8]. A commonly used regimen is 5-fluorouracil + oxaliplatin.

For palliative chemotherapy, a recommended combination is based on 5-fluorouracil. FOLFIRI (+/- cetuximab) is suggested, following colorectal regimens.

Follow up:

The median overall survival varies based on the stage and grade, with a notable trend towards the significance of the Tang classification in various series. For instance, patients presenting with peritoneal disease have a median overall survival of 25 months, while retrospective single-center case series of mixed populations report a range of 43 to 83 months [5, 9].

For patients deemed fit for further intervention, it is advisable to conduct appropriate clinical, biochemical, and imaging follow-up, tailored to the specific stage and grade. This follow-up is best managed through a colorectal Multidisciplinary Team (MDT), following the protocol for equivalent colorectal adenocarcinoma. Despite this, it's crucial to extend the follow-up duration due to the significant risk of relapse persisting beyond 5 years. Consequently, follow-up might be continued for up to 10 years, aligning with the approach taken for other gastroenteropancreatic NETs [10].

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PAGE 3 - REFERENCES

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