胃癌卵巢转移诊断和治疗中国专家共识(2021 版)解读

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摘　要:中国抗癌协会胃癌专业委员会组织专家编写了《胃癌卵巢转移诊断和治疗中国专家共识(2021 版)》,以求进一步规范胃癌卵巢转移患者的诊疗流程,改善患者预后。全文对共识中胃癌卵巢转移的诊断、分型和治疗等重点内容进行解读。
主题词:胃癌;卵巢转移;分型;综合治疗;共识
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Interpretation of the Chinese Expert Consensus on the Diagnosis and Treatment of Ovarian Metastasis from Gastric Cancer, 2021

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Abstract: The Gastric Cancer Association of Chinese Anti-Cancer Association organized experts to compile the *Chinese Expert Consensus on the Diagnosis and Treatment of Ovarian Metastasis from Gastric Cancer, 2021*, in order to further standardize the diagnosis and treatment process of patients with ovarian metastasis from gastric cancer and improve the prognosis of these patients. Now the consensus on the diagnosis, classification and treatment of ovarian metastasis from gastric cancer will be interpreted.
Subject words: gastric cancer; ovarian metastasis; classification; comprehensive therapy; consensus

胃癌是我国最常见的消化系统恶性肿瘤，远处转移是影响胃癌患者预后的主要因素，其中卵巢转移是女性患者较为常见的转移方式[1-2]。据报道,胃癌卵巢转移的发生率为 0.3%~6.7%，部分尸检研究报道的发生率高达 33.0%~43.6%[3-6]。胃癌卵巢转移的预后较其他消化道肿瘤来源的卵巢转移瘤预后差,中位生存时间仅 7~14 个月[7]。因此,胃癌卵巢转移的临床诊治仍面临着巨大挑战。

为进一步规范胃癌卵巢转移患者的诊疗流程,改善此类患者预后，中国抗癌协会胃癌专业委员会组织全国 40 余家中心 80 余位专家编写了《胃癌卵巢转移诊断和治疗中国专家共识（2021 版）》(以下简称《共识》),并于 2022 年 1 月发布[8]。该共识就胃癌卵巢转移的发病机制、诊断方式以及治疗模式进行了系统阐述，并首次提出同时性胃癌卵巢转移瘤的临床分型以及不同分型的综合治疗模式。《共识》旨在通过提高此类疾病临床诊治的合理性、临床分型的精确化和综合治疗的个体化，从而使患者达到最大临床获益。

1　胃癌卵巢转移的机制

胃癌卵巢转移的具体机制目前仍未明确，根据前期研究报道,其潜在机制可能包括种植性转移、血行转移和逆行性淋巴转移[9-10]。由于临床中部分患者

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卵巢表面较为光滑、完整或胃癌原发灶并未突破浆膜,因此种植性转移学说仍广受争议[11]。而当前认可度较高的逆行性淋巴转移学说与卵巢富含淋巴管网的解剖结构较为契合。当胃正常淋巴回流受阻时,胃癌细胞可通过淋巴逆流进入腹膜后淋巴结和盆腔淋巴结,从而导致胃癌卵巢转移[12]。因绝经前女性患者卵巢功能活跃、血供丰富,可为转移瘤提供适宜的生存环境,而继发于胃癌的卵巢肿瘤多为双侧卵巢转移,肿瘤主要侵及卵巢间质,故血行转移亦可能是其转移机制之一[13]。同时,雌、孕激素受体在胃癌卵巢转移进程中备受关注,研究表明"胃-卵巢轴"或可造成胃癌细胞器官选择转移[14-15]。鉴于胃癌卵巢转移的复杂性,《共识》指出,该过程可能是多途径综合作用所致,而非单独因素驱动。

2 胃癌卵巢转移的诊断

胃癌卵巢转移发病隐秘、早期临床症状不明显,导致其临床诊断率远低于尸检检出率。《共识》特别强调增强 CT 在胃癌卵巢转移诊断中的重要作用。增强 CT 可以明确卵巢病灶的大小和范围,并结合胃癌原发灶浸润情况进行综合评估,因此将其作为首选影像学检查手段(推荐度:高);由于经阴道超声(含多普勒超声)对生理性卵泡结构以及肿瘤囊性结构敏感性较高,可作为一种辅助检查手段;而 PET/CT 可用于评估全身转移情况以明确临床分期[16-21]。CEA、CA-724、CA-199、CA-125 等血清肿瘤标志物的异常升高也常常提示肿瘤的进展,其中 CA-125 和 CA-125/CEA 比值异常在胃癌卵巢转移诊断中具有一定临床价值[22-26]。诊断性腹腔镜探查联合脱落细胞学检查被推荐用于评估胃癌卵巢转移情况和腹膜转移范围(推荐度:高),为有转化治疗可能性患者的进一步治疗提供依据[27]。病理学和免疫组化有助于鉴别原发性和转移性卵巢肿瘤,对临床分期、治疗和预后评估等具有重要意义[10,27-28]。

3 胃癌卵巢转移的分型和治疗

为进一步实现对胃癌卵巢转移患者实行分层管理,《共识》在前期多项研究的基础上,基于原发灶和转移灶的可切除性,提出了胃癌卵巢转移中国分型(Chinese Classification of Gastric Cancer with Ovarian Metastasis,C-GCOM 分型),即将同时性胃癌卵巢转移分为Ⅰ型(可切除型)、Ⅱ型(潜在可切除型)和Ⅲ型(不可切除型)。

C-GCOM Ⅰ型为胃癌合并单纯卵巢转移,其定义为胃癌原发灶浸润深度≤T_{4a},区域淋巴结可切除(D2 或 D2+,不包括 Bulky N_2),而卵巢转移灶不合并腹腔积液、腹膜转移或脱落细胞学阳性,不伴有其他脏器转移。若胃原发灶局限于黏膜层或黏膜下层(T_1),卵巢转移瘤任意大小(Ⅰa 型),可选择胃原发灶和附件切除,术后予系统治疗。而对于 T_2 及以上患者,若卵巢转移灶最大径<5 cm(Ⅰb 型),可在系统治疗后进行原发灶和附件切除;若最大径≥5 cm(Ⅰc 型)可优先选择附件切除再予以系统治疗(推荐度:高)(附图 1)。

对于Ⅰ型的患者,预后相对较好,因此建议原发灶和转移灶行 R0 切除。对于胃原发灶,可选择胃癌根治术+D2 淋巴结清扫。由于卵巢转移灶发现时常为双侧转移,对于初始为单侧卵巢转移的年轻患者,可行对侧卵巢活检以评估保留对侧卵巢的可能性,否则建议行预防性对侧卵巢切除。术后应继续行系统治疗。

对于 C-GCOMⅡ型患者,即原发灶浸润深度为 T_{4b} 和(或)淋巴结 Bulky N_2,转移灶为脱落细胞学阳性(CY+),和(或)局限腹膜转移(PCI 评分≤6),和(或)其他单个脏器局限转移(包括局限的 No.16a2/b1 淋巴结),经充分影像学检查、诊断性腹腔镜探查和多学科诊疗讨论后,可考虑行转化治疗。对于卵巢转移瘤<5 cm,不伴有明显症状的(Ⅱa 型),可以先选择系统治疗。对于卵巢转移瘤较大(≥5 cm)或合并有中大量腹腔积液或者明显症状的(Ⅱb 型),在系统治疗前可考虑先行附件切除,以降低肿瘤耐药负荷,提高治疗疗效。系统治疗的方案选择以联合化疗为主,参考晚期胃癌的方案[29-35]。随着分子靶向药物和免疫检查点抑制剂的进展,化疗联合抗 HER2以及免疫检查点抑制剂治疗使得疾病缓解率得到提升,在晚期胃癌中有着较好的应用前景[36-40]。大部分的胃癌卵巢转移合并有腹膜转移,多项研究证实,腹腔化疗或腹腔热灌注化疗可为腹膜转移患者带来生存获益,因此对于 C-GCOM Ⅱ型的患者,腹腔化疗或腹腔热灌注化疗也是转化治疗可供选择的方案[41-43](附图 1)。

关于系统治疗的时间和手术干预的时机，指南建议，联合治疗应持续 3~6 个月，每 2~3 个周期可进行 1 次综合评估，包括治疗疗效，患者体力状态以及手术达到 R0 切除的可能性。手术介入的时机应选择在化疗有效、且尚未出现耐药时进行。关于手术范围，目前仍有一定的争议，特别是腹膜转移病灶，指南建议对于腹膜转移病灶局限瘢痕化的，行多点活检或腹膜病灶切除。对于Ⅱ型患者，即使达到完全的减瘤手术，术后仍有较高的复发转移风险。因此，术后的系统治疗还是应当借鉴晚期胃癌的治疗模式。

同时性胃癌卵巢转移 C-GCOM Ⅲ型患者胃原发灶严重外侵，与周围正常组织无法分离或包绕大血管，区域淋巴结转移固定、融合成团，或转移淋巴结不在手术可清扫范围内；转移灶伴局限腹膜转移(PCI 评分≤6)和其他脏器广泛转移，或弥漫性腹膜转移(PCI 评分>6)，伴或不伴其他脏器转移。其中将卵巢转移瘤最大径<5 cm，不伴有合并中大量腹腔积液及卵巢转移瘤所致症状定义为Ⅲa 型；若卵巢转移瘤最大径≥5 cm，或合并中大量腹腔积液或卵巢转移瘤所致症状则定义为Ⅲb 型。此型患者常合并弥漫性腹膜转移或其他脏器广泛转移，预后极差，治疗上可参照晚期胃癌治疗模式，以姑息性治疗为主(推荐度：高)，缓解患者的症状，延长其生存时间。对于卵巢转移瘤较大的患者(Ⅲb 型)，如一般情况较好，转移瘤非融合固定，可以在系统治疗前，考虑先行附件切除，以降低转移瘤负荷，减轻患者症状，提高化疗等的疗效(附图 1)。

4 结　语

卵巢转移是女性胃癌患者治疗失败的重要原因。但目前胃癌卵巢转移机制尚不明确，病情复杂，单一治疗方式往往难以获得理想的效果。《共识》在对胃癌卵巢转移患者进行充分评估的基础上，进行分类管理，制定个体化、精准化治疗策略，进而指导临床实践，改善患者预后。未来仍需要进一步探索胃癌卵巢转移发生发展及耐药的关键机制，开展一系列前瞻性多中心大样本的临床研究，从而不断提高胃癌卵巢转移的研究及诊治水平。

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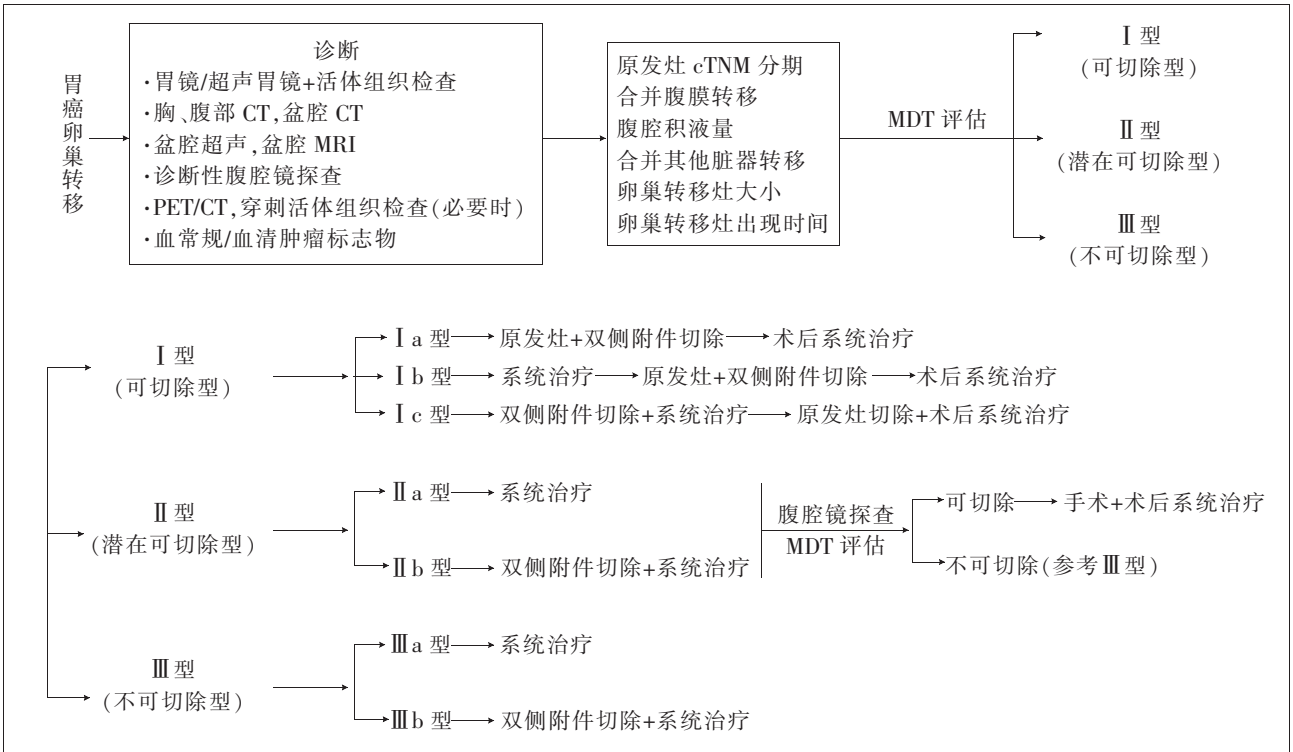

附图 1　胃癌卵巢转移初次诊治流程图[8]

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