Hans 汉斯

术前肌肉脂肪变性联合白蛋白－球蛋白评分对根治性术后胆管癌患者预后的预测价值

刘　艳*，荆　雪#

青岛大学附属医院消化内科，山东 青岛

摘　要

背景与目的：肌肉脂肪变性与多种恶性肿瘤的不良预后相关。术前白蛋白与球蛋白联合得到的白蛋白－球蛋白评分(AGS)，可预测食管癌、肺癌等恶性肿瘤的预后。本研究旨在探索术前肌肉脂肪变性联合白蛋白－球蛋白评分对胆管癌根治性切除患者的预测价值。**方法**：回顾性纳入2017年1月至2022年3月在青岛大学附属医院接受根治性切除手术的155例胆管癌患者。收集患者的血清学及影像学资料，采用Slice-O-Matic软件进行身体成分分析，Kaplan-Meier方法进行生存分析，Cox回归分析与患者总生存期和无复发生存期相关的风险因素。**结果**：本研究共纳入82例肌肉脂肪变性，73例非肌肉脂肪变性患者。Kaplan-Meier曲线显示肌肉脂肪变性与总生存期和无复发生存期相关(P = 0.022和P = 0.017)，高AGS组患者的总生存期和无复发生存期明显短于低AGS组患者(P = 0.015和P = 0.009)。同时存在高AGS和肌肉脂肪变性的患者生存期和无复发生存期最短(P = 0.005和P = 0.002)。**结论**：本研究表明，对于接受根治性切除手术的胆管细胞癌患者，术前存在肌肉脂肪变性且高白蛋白－球蛋白评分时，预后最差。以上提示临床医生尽早开展营养支持以及干预肌肉衰减的治疗。

关键词

胆管细胞癌，肌肉脂肪变性，白蛋白－球蛋白评分，根治性手术，预后

Prognostic Value of Preoperative Myosteatosis Combined with Albumin-Globulin Score in Patients with Cholangiocarcinoma after Radical Surgery

Yan Liu*, Xue Jing#

Department of Gastroenterology, The Affiliated Hospital of Qingdao University, Qingdao Shandong

*第一作者。

#通讯作者。

Abstract

Background and Purpose: Myosteatosis is associated with poor prognosis of various malignancies. The albumin-globulin score (AGS) obtained by the combination of albumin and globulin before operation can predict the prognosis of malignant tumors such as esophageal cancer and lung cancer. The objective of this study was to explore the predictive value of preoperative myosteatosis combined with albumin-globulin score in patients undergoing radical cholangiocarcinoma resection. Methods: A total of 155 patients with cholangiocarcinoma who underwent radical resection in the Affiliated Hospital of Qingdao University from January 2017 to March 2022 were retrospectively included. Serological and imaging data of the patients were collected. Slice-O-Matic software was used for body composition analysis, Kaplan-Meier method for survival analysis, and Cox regression analysis was performed to analyze the risk factors associated with overall survival and relapse-free survival of the patients. Results: A total of 82 patients with myosteatosis and 73 patients with non-myosteatosis were included in this study. Kaplan-Meier curve showed that myosteatosis was correlated with overall survival and relapse-free survival (P = 0.022 and P = 0.017), and the overall survival and relapse-free survival of patients with high AGS were significantly shorter than those in patients with low AGS (P = 0.015 and P = 0.009). Patients with both high AGS and myosteatosis had the shortest survival and relapse-free survival (P = 0.005 and P = 0.002). Conclusions: This study showed that patients with cholangiocarcinoma who underwent radical resection had the worst prognosis when myosteatosis and high albumin-globulin score were present before surgery. These results suggest that clinicians should start nutritional support and intervention therapy for muscle decay as early as possible.

Keywords

Cholangiocarcinoma, Myosteatosis, Albumin-Globulin Score, Radical Surgery, Prognosis

1. 引言

肌肉脂肪变性是细胞浆内甘油三酯(中性脂肪)的蓄积，常常由营养障碍、感染、中毒或缺氧等引起，多发生于代谢旺盛、耗氧多的组织，如肝细胞、心肌纤维、肾小管上皮等[1]。肌肉脂肪变性是多种肌肉相关病变的主要病理特征，与胃癌、肺癌、胰腺癌、慢性肝病、膀胱癌等多种疾病的严重程度及预后相关[2] [3] [4] [5] [6]。胆管细胞癌患者由于消耗增加，肝脏储备功能差，极易出现消瘦、乏力、营养不良的状态，发生肌肉脂肪变性、肌肉减少症的可能性也会增加[7]。白蛋白是正常人体血清中的主要蛋白质，用于评估人体的营养状况[8]。当肝脏合成功能障碍时，白蛋白水平会明显下降。球蛋白与白蛋白一样，都是机体内非常重要的免疫物质，能有效的提升机体免疫力，对抗各种感染传染性疾病[9]。白蛋白与球蛋白联合的白蛋白 – 球蛋白评分(AGS)，与多发性骨髓瘤、肝内胆管细胞癌、肝细胞癌肝移植等患者的预后有着密切的关系[9] [10]。目前，对于肌肉脂肪变性以及白蛋白 – 球蛋白评分对于接受根治性切除手术胆管细胞癌患者的预测价值如何尚无明确研究。本文回顾性分析接受根治性切除手术的胆管细胞癌患者的白蛋白 – 球蛋白评分(AGS)与肌肉脂肪变性情况，研究其与预后之间的关系。

2. 材料与方法

1) 患者

在这项回顾性研究中，共收集了 2017 年 1 月至 2022 年 3 月在青岛大学附属医院接受根治性外科切除手术的 155 例胆管癌患者资料。纳入标准如下：a) 接受根治性切除手术，且术后病理为胆管细胞癌；b) 术前未接受辅助治疗，包括局部及全身放化疗，或其他抗癌治疗；c) 可获得完整的术前影像学资料用于分析身体成分；d) 术前有完整的白蛋白、球蛋白等血清学数据；e) 可完成随访者。随访形式为电话随访，截止到 2022 年 11 月。本研究排除了合并其他肿瘤和无法完成随访的患者。本研究经青岛大学附属医院伦理委员会(批准文号 QYFY WZLL 28042)批准。

2) 临床资料收集

从青岛大学附属医院电子医疗系统中检索所有患者的临床数据和实验室参数。收集胆管癌患者接受根治性切除手术前的白蛋白和球蛋白数据，根据文献参考标准定义白蛋白–球蛋白评分(AGS)：白蛋白 > 41.7 g/L 和球蛋白 ≤28.6 g/L 的患者定义为 AGS 0，白蛋白 ≤41.7 g/L 和球蛋白 >28.6 g/L 的患者定义为 AGS 2，其余患者定义为 AGS 1 [11]。AGS 1 和 AGS 2 的患者为高 AGS 组，AGS 0 的患者为低 AGS 组 [9]。另外我们还收集了肿瘤相关的临床病理特征，包括肿瘤最大直径、分化程度、神经侵犯、脉管侵犯、淋巴结转移、有无胆系结石等。研究的主要终点为总生存期(OS)，即从手术切除日期到最后一次随访或临床死亡的时间，次要终点是无复发生存期(RFS)，为手术日期至随访截止或肿瘤复发的时间。

3) 影像学身体成分分析

收集患者术前 1 月内的电子计算机断层扫描(CT)资料，采用 Slice-O-Matic 软件对第三腰椎水平的各种身体组织成分进行影像学分析(图 1)，由两名研究人员进行盲法检查。不同组织特定的 HU 阈值如下：骨骼肌组织为−29 至+150 HU，皮下脂肪为−190 HU 至−30 HU，内脏脂肪为−150 至−50 HU，肌内脂肪为−190 HU 至−30 HU [12]。肌肉脂肪变性通过平均骨骼肌衰减来评估，定义标准如下：$BMI < 25 \ kg/m^2$ 的患者 SMA < 41 HU，$BMI \geq 25 \ kg/m^2$ 的患者 SMA < 33 HU [13]。根据以上标准将所有患者分为肌肉脂肪变性组和非肌肉脂肪变性组。

Figure 1. Computes tomography (CT) was used to evaluate muscle quantity and mass in the third lumbar vertebra of the spine (the red part)
图 1. 计算机断层扫描(CT)评价脊柱第三腰椎的肌肉数量和质量(红色部分)

4) 统计分析

所有数据均通过 SPSS (version 26.0, IBM, Armonk, NY, USA)软件进行统计学分析。根据白蛋白–球蛋白评分(AGS)和肌肉脂肪变性的诊断标准对所有患者进行分组。绘制不同分组下相应的 Kaplan-Meier

曲线，利用 Log-rank 检验进行统计检验。通过单因素和多因素 Cox 比例风险模型分析影响总生存期的无复发生存期的潜在因素，显示危险比(HR)和 95%可信区间(CI 95%)。双侧 P < 0.05 认为具有统计学意义。

3. 结果

1) 患者的基线特征

根据纳入和排除标准，我们的研究共纳入 155 例病理诊断为胆管细胞癌的患者，由研究人员进行影像学分析，基于文献的诊断标准，将所有患者分为肌肉脂肪变性组 82 例，非肌肉脂肪变性组 73 例。患者的基线资料如表格 1 所示。在人口学方面，肌肉脂肪变性组患者平均年龄为 64.22 ± 7.94，高于非肌肉脂肪变性组平均年龄 58.26 ± 9.81，而且肌肉脂肪变性组男性占比更高(75.3% vs. 40.2%)，差异均具有统计学意义(P = 0.000)。根据 WHO 标准，非肌肉脂肪变性组体重偏高(BMI ≥ 25 kg/m^2)者比例高于肌肉脂肪变性组，差异有统计学意义(56.2% vs. 25.6%, P = 0.000)。肌肉脂肪变性组肿瘤高分化者占比例更高(50.0% vs. 42.5%, P = 0.002)。与肌肉脂肪变性组相比，非肌肉脂肪变性组患者吸烟史、饮酒史的发生率更高(37.0% vs. 17.1%，P = 0.005 和 30.1% vs. 15.9%，P = 0.034)，糖尿病发生率较低(9.6% vs. 22.0%，P = 0.037)。在血清学方面，与非肌肉脂肪变性组相比较，肌肉脂肪变性组患者白蛋白水平更低(P = 0.002)，血红蛋白较低(P = 0.000)，但 CA125 水平更高(P = 0.032)。在身体成分分析方面，肌肉脂肪变性患者同时出现肌肉减少症的比例更高(57.3% vs. 38.4%, P = 0.018)，肌间脂肪组织面积在统计学上增加了(7.99 ± 5.02 vs. 5.84 ± 3.68, P = 0.010)。而与肌肉脂肪变性组相比，非肌肉脂肪变性组患者的骨骼肌质量指数(SMI)、平均骨骼肌衰减(SMA)、内脏与皮下脂肪组织比值(VSR)在统计学上均显著增加了(P < 0.05)。

2) 肌肉脂肪变性、白蛋白 − 球蛋白评分及其联合的预后价值

根据诊断标准，我们将所有患者进行分组：肌肉脂肪变性组 82 例，非肌肉脂肪变性组 73 例；低 AGS 组(AGS = 0) 37 例，高 AGS 组(AGS = 1/2) 118 例。利用统计学软件分别对总生存期和无复发生存期进行分析，如图 2 所示。与非肌肉脂肪变性组患者相比，肌肉脂肪变性组患者的总生存期较短(中位生存时间，26.5 月 vs. 43.9 月，P = 0.022) (图 2(a))，无复发生存期也更差(中位复发时间，26.4 月 vs. 39.7 月，P = 0.017) (图 2(b))。高 AGS 组患者的总生存期明显短于低 AGS 组(中位生存时间，34.3 月 vs. 41.2 月，P = 0.015) (图 2(c))，无复发生存期也更短(中位复发时间，33.0 月 vs. 39.7 月，P = 0.009) (图 2(d))。
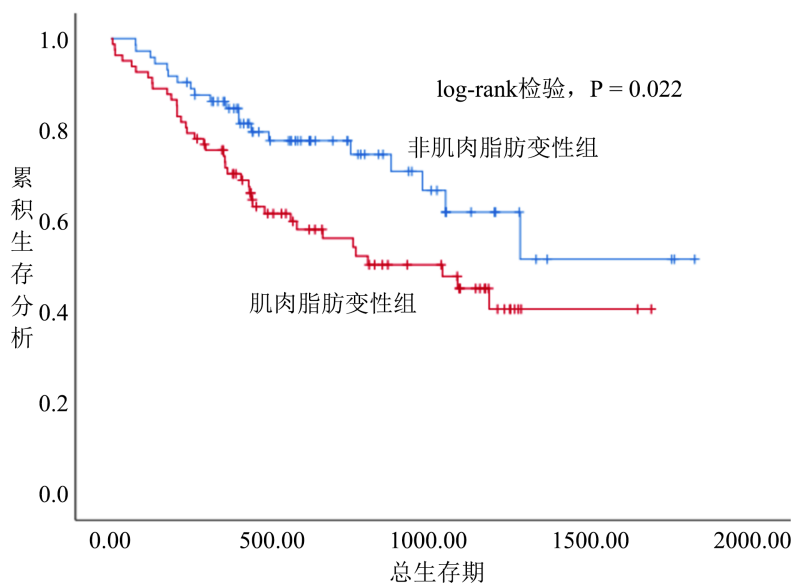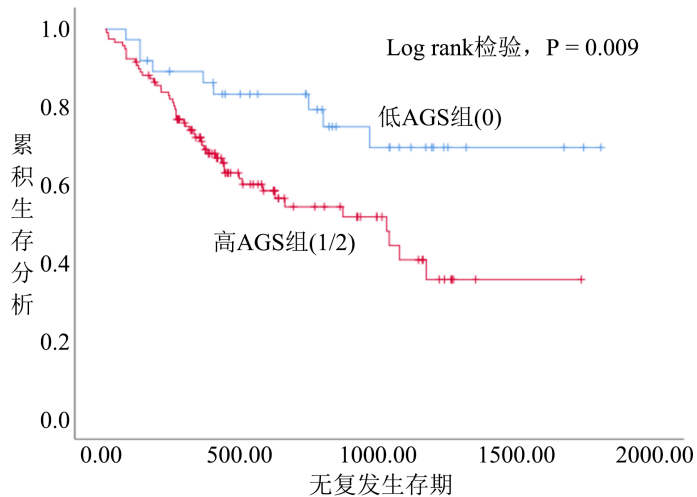

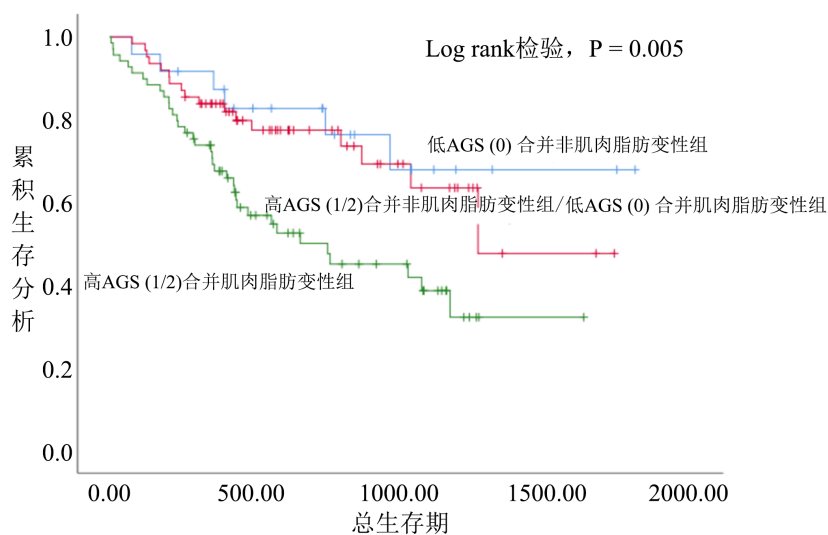(a) 肌肉脂肪变性组和非肌肉脂肪变性组患者总生存期的曲线比较
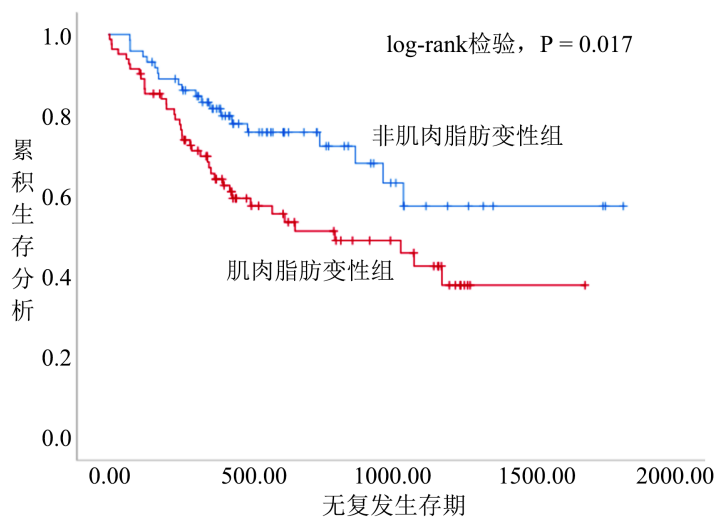
(b) 肌肉脂肪变性组和非肌肉脂肪变性组患者无复发生存期的曲线比较
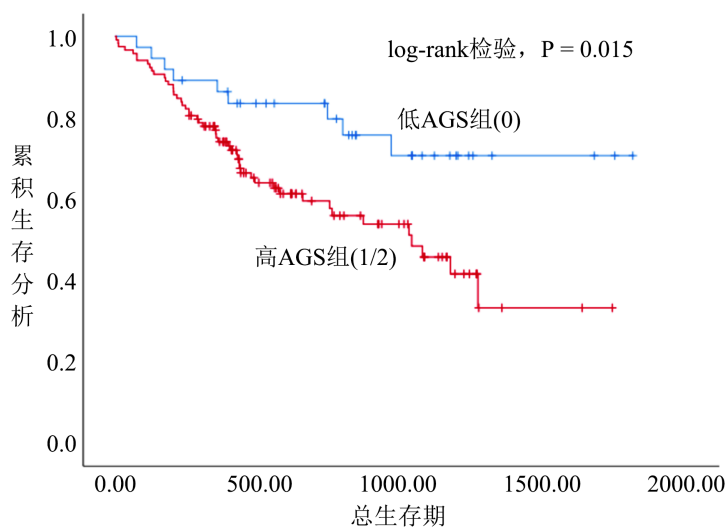
(c) 低 AGS 组和高 AGS 组患者总生存期的曲线比较

(d) 低 AGS 组和高 AGS 组患者无复发生存期的曲线比较

(e) 有无肌肉脂肪变性合并 AGS 分组的总生存期曲线
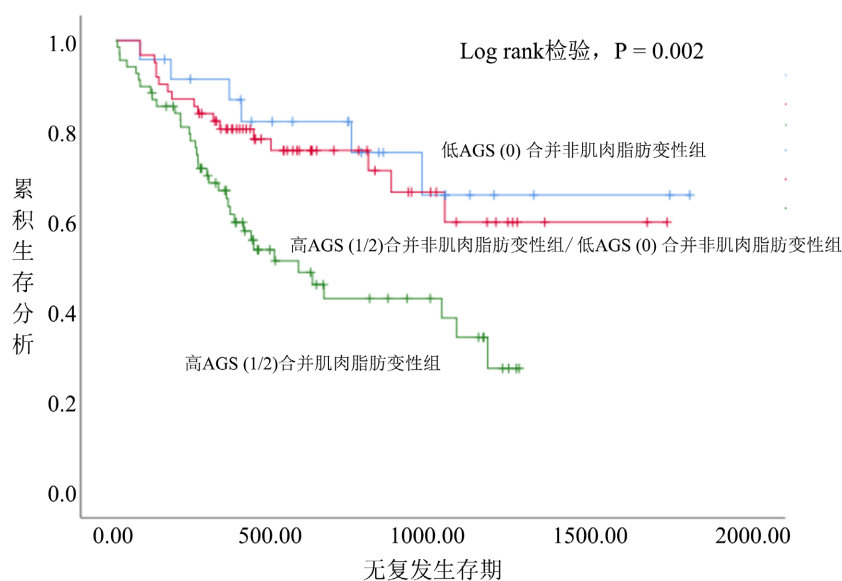
(f) 有无肌肉脂肪变性合并 AGS 分组的无复发生存期曲线

Figure 2. Survival analysis curve
图 2. 生存分析曲线

另外，我们将肌肉脂肪变性与白蛋白 − 球蛋白评分两个指标联合，以研究此联合指标对胆管细胞癌患者预后的预测价值。如图 2(e)、图 2(f)所示，与其他组相比，同时出现高 AGS 和肌肉脂肪变性的患者累计生存概率最低，中位生存期为 21.8 月，中位无复发生存期为 16.7 月，差异具有统计学意义(P = 0.005 和 P = 0.002)。

3) 总生存期和无复发生存期的 Cox 回归分析

在单因素 Cox 回归分析中，年龄(HR 1.033, P = 0.030)，淋巴结转移(HR 3.356, P = 0.000)，白蛋白(HR 0.925, P = 0.000)，碱性磷酸酶(HR 1.001, P = 0.007)，CA125 (HR 1.001, P = 0.004)和肌肉脂肪变性(HR 1.858, P = 0.025)是总生存期的预测指标。将单因素回归分析中有统计学意义的指标纳入多因素回归，发现仅淋巴结转移(HR 2.891, P = 0.000)和白蛋白(HR 0.945, P = 0.038)与总生存期独立相关(图 2)。

关于无复发生存期，在单因素回归分析中，年龄(HR 1.032, P = 0.032)，淋巴结转移(HR 3.349, P = 0.000)，白蛋白(HR 0.922, P = 0.000)，碱性磷酸酶(HR 1.001, P = 0.008)，CA125(HR 1.002, P = 0.008)，肌肉脂肪变性(HR 1.907, P = 0.019)和脉管侵犯(HR 1.714, P = 0.041)是总复发生存期的预测指标。将以上有意义的指标纳入多因素回归分析，白蛋白(HR 0.936, P = 0.014)、淋巴结转移(HR 2.763, P = 0.000)和脉管侵犯(HR 1.811, P = 0.033)与无复发生存期独立相关。

4. 讨论

肌肉脂肪变性被定义为肌细胞间和肌细胞内脂肪组织分布异常，是多种肌肉相关病变的主要病理特征，如 2 型糖尿病胰岛素抵抗、肌肉退行性病变、肝硬化等，且脂肪含量越高，病情越严重[14] [15] [16]。作为肌肉病变的一种类型，活组织病理是确诊的金标准，但由于取材的侵入性，临床开展难度大，逐渐出现了影像学评估的方式，即可通过第三腰椎水平的电子计算机断层扫描(CT)图像来测定，主要衡量指标是平均骨骼肌衰减(SMA) [17]。

目前关于肌肉脂肪变性对疾病预后的研究得到了越来越多的关注，已有多项研究表明肌肉脂肪变性对恶性肿瘤的预后具有负面作用，潜在的发生机制主要围绕胰岛素抵抗、组织蛋白酶促进脂肪组织脂解、巨噬细胞分泌促炎因子和线粒体氧化损伤等[13] [18] [19] [20]。组织蛋白酶 D 是一种天冬氨酰内蛋白酶，在恶性肿瘤中可过度表达，促进细胞内蛋白质代谢降解，诱导细胞内脂质积聚，从而导致肌肉脂肪变性[21]。机体发生肌肉脂肪变性时，脂质代谢产物如二酰基甘油可促进氧化应激，并介导胰岛素抵抗，使得肿瘤细胞生存增值，骨骼肌胰岛素不敏感，从而增加脂质积累[18] [22]。肌肉脂肪变性可促进炎症反应，引起机体代谢紊乱，改变营养状态，肌肉脂肪变性极易出现在营养不良的患者中[23] [24]。我们的研究与Isabella Lurje 等人的研究结果一致，在研究队列中，有超过一半(52.9%)的胆管细胞癌患者发生了肌肉脂肪变性，且此类患者的总生存期和无复发生存期明显缩短[25]。研究发现肌肉脂肪变性的程度会随着年龄增加而加重，这点在我们的研究中也有体现，肌肉脂肪变性组患者平均年龄高于非肌肉脂肪变性组[26]。

肌肉减少症是指与增龄相关的骨骼肌质量和肌肉力量或躯体功能下降，与肌肉脂肪变性一样，均可通过计算机断层扫描(CT)来评估，主要衡量指标是骨骼肌指数(SMI) [27] [28]。已有多项研究表明肌肉减少症与结直肠癌、胰腺癌、胃癌等恶性肿瘤患者的不良预后相关[4] [28] [29]。骨骼肌减少症的发生机制可能与神经源性炎症细胞因子、线粒体功能障碍以及氧化应激等因素有关[30] [31] [32]。

机体的营养状态对癌症患者的预后有着非常强烈的影响，血清白蛋白和球蛋白通常是反映系统营养状况和免疫炎症的重要物质[10] [33]。将白蛋白与球蛋白联合得到的新模型即白蛋白 - 球蛋白评分(AGS)，已被证实是肺癌、食管癌等多种恶性肿瘤不良预后的预测因子[11] [34] [35]。Hui Li 等人研究将术前 AGS 与骨骼肌指数(SMI)联合得到的新指标CAS可预测接受手术切除的肝内胆管癌患者的预后[36]。该研究发现 AGS 与肝内胆管细胞癌患者的中位生存时间有显著相关性，在区分不同预后的肝内胆管细胞癌患者中发挥很大作用。但据我们所知，尚未有研究探索术前 AGS 联合肌肉脂肪变性的预测价值。

而我们的研究首次发现术前出现肌肉脂肪变性时，同时合并高 AGS，预测价值更高，患者的预后会更差，生存期大大缩短。当然，这项研究不可避免的存在一些局限性：首先，研究属于单中心研究，随访时间短、队列人数少，代表性不强，在未来需要扩大研究的数据范围，进行多中心研究。其次，这是一项回顾性研究，无法排除回忆偏倚的影响，需要进行前瞻性研究来验证。

5. 结论

本研究发现对于接受根治性切除手术的胆管细胞癌患者，术前同时出现肌肉脂肪变性和高白蛋白 - 球蛋白评分(AGS)时，生存期和无复发生存期会大大缩短，预后更差。这一发现可以帮助临床医生更好地

评估胆管细胞癌患者的营养状况及预后，在未来的研究中，有必要进行更多的机制探索。

伦理学审查

基金项目

参考文献

[1] Cankurtaran, R.E., Güneş, Y.C., Dirican, E., *et al*. (2023) Sarcopenia and Myosteatosis Assessed by Magnetic Resonance Enterography May Predict Negative Outcomes in Patients with Crohn's Disease. *Turkish Journal of Gastroenterology*, **34**, 839-849. https://doi.org/10.5152/tjg.2023.22644

[2] Petric, M., Jordan, T., Karteek, P., *et al*. (2023) Radiological Assessment of Skeletal Muscle Index and Myosteatosis and Their Impact Postoperative Outcomes after Liver Transplantation. *Radiology and Oncology*, **57**, 168-177. https://doi.org/10.2478/raon-2023-0025

[3] Feng, S., Mu, H., Hou, R., *et al*. (2022) Prognostic Value of Myosteatosis in Patients with Lung Cancer: A Systematic Review and Meta-Analysis. *International Journal of Clinical Oncology*, **27**, 1127-1138. https://doi.org/10.1007/s10147-022-02181-1

[4] Kim, D.W., Ahn, H., Kim, K.W., *et al*. (2022) Prognostic Value of Sarcopenia and Myosteatosis in Patients with Resectable Pancreatic Ductal Adenocarcinoma. *Korean Journal of Radiology*, **23**, 1055-1066. https://doi.org/10.3348/kjr.2022.0277

[5] Fang, T., Gong, Y. and Wang, Y. (2023) Prognostic Values of Myosteatosis for Overall Survival in Patients with Gastric Cancers: A Meta-Analysis with Trial Sequential Analysis. *Nutrition*, **105**, Article ID: 111866. https://doi.org/10.1016/j.nut.2022.111866

[6] Engelmann, S.U., Pickl, C., Haas, M., *et al*. (2023) Body Composition of Patients Undergoing Radical Cystectomy for Bladder Cancer: Sarcopenia, Low Psoas Muscle Index, and Myosteatosis Are Independent Risk Factors for Mortality. *Cancers* (*Basel*), **15**, Article No. 1778. https://doi.org/10.3390/cancers15061778

[7] Ryan, A.M., Power, D.G., Daly, L., *et al*. (2016) Cancer-Associated Malnutrition, Cachexia and Sarcopenia: The Skeleton in the Hospital Closet 40 Years Later. *Proceedings of the Nutrition Society*, **75**, 199-211. https://doi.org/10.1017/S002966511500419X

[8] Xie, D., Lu, P.L., Xu, W., *et al*. (2023) Correlation of Serum Albumin Level on Postoperative Day 2 with Hospital Length of Stay in Patients Undergoing Emergency Surgery for Perforated Peptic Ulcer. *World Journal of Gastrointestinal Surgery*, **15**, 1434-1441. https://doi.org/10.4240/wjgs.v15.i7.1434

[9] Cai, Y., Zhao, Y., Dai, Q., *et al*. (2021) Prognostic Value of the Albumin-Globulin Ratio and Albumin-Globulin Score in Patients with Multiple Myeloma. *Journal of International Medical Research*, **49**. https://doi.org/10.1177/0300060521997736

[10] Huang, Y., Wang, N., Xu, L., *et al*. (2023) Albumin-Globulin Score Combined with Skeletal Muscle Index as a Novel Prognostic Marker for Hepatocellular Carcinoma Patients Undergoing Liver Transplantation. *Journal of Clinical Medicine*, **12**, Article No. 2237. https://doi.org/10.3390/jcm12062237

[11] Li, X., Qin, S., Sun, X., *et al*. (2018) Prognostic Significance of Albumin-Globulin Score in Patients with Operable Non-Small-Cell Lung Cancer. *Annals of Surgical Oncology*, **25**, 3647-3659. https://doi.org/10.1245/s10434-018-6715-z

[12] Mitsiopoulos, N., Baumgartner, R.N., Heymsfield, S.B., *et al*. (1998) Cadaver Validation of Skeletal Muscle Measurement by Magnetic Resonance Imaging and Computerized Tomography. *Journal of Applied Physiology* (1985), **85**, 115-122. https://doi.org/10.1152/jappl.1998.85.1.115

[13] Ebadi, M., Tsien, C., Bhanji, R.A., *et al*. (2022) Myosteatosis in Cirrhosis: A Review of Diagnosis, Pathophysiological Mechanisms and Potential Interventions. *Cells*, **11**, Article No. 1216. https://doi.org/10.3390/cells11071216

[14] Zeng, X., Shi, Z.W., Yu, J.J., *et al*. (2023) Skeletal Muscle Alterations Indicate Poor Prognosis in Cirrhotic Patients: A Multicenter Cohort Study in China. *Hepatology International*. https://doi.org/10.1007/s12072-023-10497-x

[15] Geladari, E., Alexopoulos, T., Kontogianni, M.D., *et al*. (2023) The Presence of Myosteatosis Is Associated with Age, Severity of Liver Disease and Poor Outcome and May Represent a Prodromal Phase of Sarcopenia in Patients with Liver Cirrhosis. *Journal of Clinical Medicine*, **12**, Article No. 3332. https://doi.org/10.3390/jcm12093332

[16] Kiefer, L.S., Fabian, J., Rospleszcz, S., *et al.* (2018) Assessment of the Degree of Abdominal Myosteatosis by Magnetic Resonance Imaging in Subjects with Diabetes, Prediabetes and Healthy Controls from the General Population. *European Journal of Radiology*, **105**, 261-268. https://doi.org/10.1016/j.ejrad.2018.06.023

[17] Ahn, H., Kim, D.W., Ko, Y., *et al.* (2021) Updated Systematic Review and Meta-Analysis on Diagnostic Issues and the Prognostic Impact of Myosteatosis: A New Paradigm Beyond Sarcopenia. *Ageing Research Reviews*, **70**, Article ID: 101398. https://doi.org/10.1016/j.arr.2021.101398

[18] Scopel Poltronieri, T., De Paula, N.S. and Chaves, G.V. (2022) Skeletal Muscle Radiodensity and Cancer Outcomes: A Scoping Review of the Literature. *Nutrition in Clinical Practice*, **37**, 1117-1141. https://doi.org/10.1002/ncp.10794

[19] Aleixo, G.F.P., Shachar, S.S., Nyrop, K.A., *et al.* (2020) Myosteatosis and Prognosis in Cancer: Systematic Review and Meta-Analysis. *Critical Reviews in Oncology/Hematology*, **145**, Article ID: 102839. https://doi.org/10.1016/j.critrevonc.2019.102839

[20] Cespiati, A., Meroni, M., Lombardi, R., *et al.* (2022) Impact of Sarcopenia and Myosteatosis in Non-Cirrhotic Stages of Liver Diseases: Similarities and Differences across Aetiologies and Possible Therapeutic Strategies. *Biomedicines*, **10**, Article No. 182. https://doi.org/10.3390/biomedicines10010182

[21] Ding, L., De Munck, T.J.I., Oligschlaeger, Y., *et al.* (2021) Myosteatosis in NAFLD Patients Correlates with Plasma Cathepsin D. *Biomolecular Concepts*, **12**, 27-35. https://doi.org/10.1515/bmc-2021-0004

[22] Hamrick, M.W., Mcgee-Lawrence, M.E. and Frechette, D.M. (2016) Fatty Infiltration of Skeletal Muscle: Mechanisms and Comparisons with Bone Marrow Adiposity. *Frontiers in Endocrinology* (*Lausanne*), **7**, Article No. 69. https://doi.org/10.3389/fendo.2016.00069

[23] Lutz, C.T. and Quinn, L.S. (2012) Sarcopenia, Obesity, and Natural Killer Cell Immune Senescence in Aging: Altered Cytokine Levels as a Common Mechanism. *Aging* (*Albany NY*), **4**, 535-546. https://doi.org/10.18632/aging.100482

[24] Chen, W.Z., Shen, Z.L., Zhang, F.M., *et al.* (2022) Prognostic Value of Myosteatosis and Sarcopenia for Elderly Patients with Colorectal Cancer: A Large-Scale Double-Center Study. *Surgery*, **172**, 1185-1193. https://doi.org/10.1016/j.surg.2022.05.031

[25] Lurje, I., Uluk, D., Pavicevic, S., *et al.* (2023) Body Composition Is Associated with Disease Aetiology and Prognosis in Patients Undergoing Resection of Intrahepatic Cholangiocarcinoma. *Cancer Medicine*, **12**, 17569-17580. https://doi.org/10.1002/cam4.6374

[26] Correa-De-Araujo, R., Addison, O., Miljkovic, I., *et al.* (2020) Myosteatosis in the Context of Skeletal Muscle Function Deficit: An Interdisciplinary Workshop at the National Institute on Aging. *Frontiers in Physiology*, **11**, Article No. 963. https://doi.org/10.3389/fphys.2020.00963

[27] Maslennikov, R., Alieva, A., Poluektova, E., *et al.* (2023) Sarcopenia in Cirrhosis: Prospects for Therapy Targeted to Gut Microbiota. *World Journal of Gastroenterology*, **29**, 4236-4251. https://doi.org/10.3748/wjg.v29.i27.4236

[28] Stretch, C., Aubin, J.M., Mickiewicz, B., *et al.* (2018) Sarcopenia and Myosteatosis Are Accompanied by Distinct Biological Profiles in Patients with Pancreatic and Periampullary Adenocarcinomas. *PLOS ONE*, **13**, E0196235. https://doi.org/10.1371/journal.pone.0196235

[29] Salavatizadeh, M., Soltanieh, S., Radkhah, N., *et al.* (2023) The Association between Skeletal Muscle Mass Index (SMI) and Survival after Gastrectomy: A Systematic Review and Meta-Analysis of Cohort Studies. *European Journal of Surgical Oncology*, **49**, Article ID: 106980. https://doi.org/10.1016/j.ejso.2023.07.006

[30] Zhang, H., Qi, G., Wang, K., *et al.* (2023) Oxidative Stress: Roles in Skeletal Muscle Atrophy. *Biochemical Pharmacology*, **214**, Article ID: 115664. https://doi.org/10.1016/j.bcp.2023.115664

[31] Jang, J.Y., Kim, D. and Kim, N.D. (2023) Pathogenesis, Intervention, and Current Status of Drug Development for Sarcopenia: A Review. *Biomedicines*, **11**, Article No. 1635. https://doi.org/10.3390/biomedicines11061635

[32] Okugawa, Y., Kitajima, T., Yamamoto, A., *et al.* (2022) Clinical Relevance of Myopenia and Myosteatosis in Colorectal Cancer. *Journal of Clinical Medicine*, **11**, Article No. 2617. https://doi.org/10.3390/jcm11092617

[33] Chen, Z., Song, C., Yao, Z., *et al.* (2022) Associations between Albumin, Globulin, Albumin to Globulin Ratio and Muscle Mass in Adults: Results from the National Health and Nutrition Examination Survey 2011-2014. *BMC Geriatrics*, **22**, Article No. 383. https://doi.org/10.1186/s12877-022-03094-4

[34] Zhang, F., Sun, P., Wang, Z.Q., *et al.* (2016) Low Preoperative Albumin-Globulin Score Predicts Favorable Survival in Esophageal Squamous Cell Carcinoma. *Oncotarget*, **7**, 30550-30560. https://doi.org/10.18632/oncotarget.8868

[35] Chen, L., Yu, G., Zhao, W., *et al.* (2023) A Possible Combined Appraisal Pattern: Predicting the Prognosis of Patients after Esophagectomy. *World Journal of Surgical Oncology*, **21**, Article No. 155. https://doi.org/10.1186/s12957-023-03020-x

[36] Li, H., Dai, J., Lan, T., *et al.* (2021) Combination of Albumin-Globulin Score and Skeletal Muscle Index Predicts Long-Term Outcomes of Intrahepatic Cholangiocarcinoma Patients after Curative Resection. *Clinical Nutrition*, **40**, 3891-3900. https://doi.org/10.1016/j.clnu.2021.04.038