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# SARCOPENIA IS ASSOCIATED WITH SEVERE POSTOPERATIVE COMPLICATIONS IN GASTRIC CANCER PATIENTS UNDERGOING GASTRECTOMY: A HOSPITAL BASED PROSPECTIVE OBSERVATIONAL STUDY IN SUB-HIMALAYAN REGION

**Dr. Ishan Barotra[1]*, Dr. Ashish Katoch[2], Dr. Puneet Mahajan[3] and Dr. Rashpal Singh Thakur[4]**

[1,2]Junior Resident, Department of General Surgery, Indira Gandhi Medical College Shimla Himachal Pradesh.
[3]Professor, Department of General Surgery, Indira Gandhi Medical College Shimla Himachal Pradesh.
[4]Assistant Professor(Surgical Oncology), Department of General Surgery, Indira Gandhi Medical College Shimla Himachal Pradesh.

***Corresponding Author: Dr. Ishan Barotra**

Junior Resident, Department of General Surgery, Indira Gandhi Medical College Shimla Himachal Pradesh.

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## ABSTRACT

**Background:** Malignancy is a secondary cause of sarcopenia, which is associated with impaired cancer treatment outcomes. The aim of this study was to investigate postoperative complications between sarcopenic and non-sarcopenic patients of resectable gastric cancer undergoing gastrectomy. There is very limited data available from sub-Himalayan belt of northern India, hence the present study was planned to know the association of sarcopenia with postoperative complications in gastric cancer patients undergoing gastrectomy. **Methods:** A hospital based prospective observational study was conducted in the Department of General Surgery of a tertiary care hospital in Shimla, Himachal Pradesh. All patients who reported to Department of Surgery during the study period of 1st September 2021 to 30th September 2022 with diagnosis of gastric cancer were considered for the study. **Results:** Forty-one patients were included in the study and had a mean age of 60.66± 12.93 years. Sarcopenia was detected in 18(43.90%) patients based on EWGSOP2 (The European Working Group on Sarcopenia in Older People 2) recommendations. The mean age was 65.94 years in the sarcopenic group (SG) and 55.49 years in the non-sarcopenic group. The mean SMI(Skeletal Muscle Index) was 44.08±8.93cm²/m² and 46.19±9.13cm²/m² in the SG and NSG, respectively. The mean body mass index (BMI) was lower in the sarcopenic group than in the nonsarcopenic group (19.64 ± 3.36 vs. 20.18± 3.38 kg/m$^2$). Post operative complications based on Clavien Dindo classification were significantly higher in the sarcopenic group than in the non-sarcopenic group (66.6 % vs. 40 %; P = 0.03). **Conclusions:** Preoperative sarcopenia as defined by the EWGSOP2 recommendations is a risk factor for severe postoperative complications in gastric cancer patients undergoing gastrectomy.

**KEYWORDS:** Sarcopenia _ Postoperative complication _ Gastric cancer _ Gastrectomy.

## INTRODUCTION

Aging is associated with progressive, systematic loss of skeletal muscle mass (SM) and gradual changes in body composition. Since Rosenberg[1] coined the term "sarcopenia" in 1989 to describe this age-related, inescapable occurrence, the term has become widely recognized as a new concept in disease. The concept of sarcopenia was recently expanded to include loss of muscle strength and functional impairment in addition to loss of muscle mass by the European Working Group on Sarcopenia in Older People (EWGSOP)[2] and the Asian Working Group for Sarcopenia.[3] These working groups have designed a new algorithm for assessing sarcopenia. The prevalence of age-related sarcopenia based on the EWGSOP algorithm in elderly community-dwelling residents in Japan (n = 4811) was reported to be 8.2 % for men and 6.8 % for women.[4] Malnutrition, inactivity, and a number of illnesses can all contribute to sarcopenia.[5,6] Excessive systemic inflammatory response, especially in cancer patients, can lead to insulin resistance, hypercatabolism of proteins, and metabolic abnormalities.[7,8] Sarcopenia is therefore expected to be more common among cancer patients than in the senior population as a whole. Moreover, a number of studies have demonstrated that insufficient protein and calorie intake among older persons who live in the community are separate risk factors for sarcopenia.[9,10] Compared to other cancer patients, gastric cancer patients may have more severe nutritional depletion due to poor oral intake related to disease-specific symptoms, which could raise the prevalence of sarcopenia.

It is yet unknown how much sarcopenia affects cancer patients, despite the fact that it is well known to be a risk

factor for functional limitation, physical disability, a decline in quality of life, and eventually mortality.[2] Sarcopenia's impact on cancer patients' treatment outcomes has been the subject of extensive research recently; it has been shown that sarcopenia is independently linked to poor outcomes following surgery, both short- and long-term[11–18], as well as an increased risk of toxicity from chemotherapy.[21–23] There is very limited data available from sub-Himalayan belt of northern India, hence the present study was planned to know the association of sarcopenia with postoperative complications in gastric cancer patients undergoing gastrectomy.

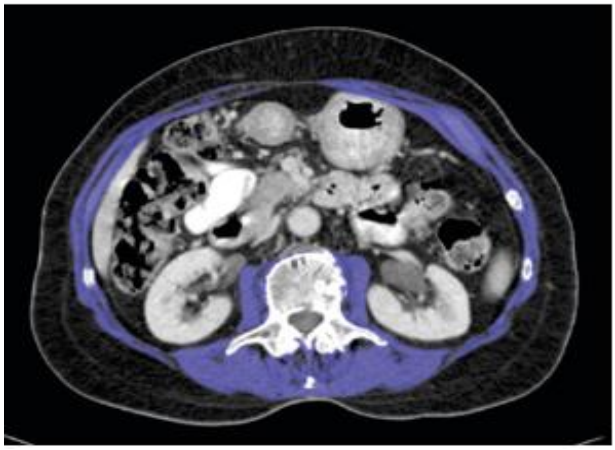
## MATERIAL AND METHODS

A hospital based prospective observational study was conducted in the department of surgery of a tertiary care hospital in Shimla, Himachal Pradesh between September 2021 to September 2022., a total of 41 gastric cancer patients reported to Department of General Surgery IGMC SHIMLA. We excluded patients who were not willing for surgery in surgical operable cases and patients with spinal deformity, quadriplegia,spinal muscular atrophy.

We investigated the postoperative complications between sarcopenic and non-sarcopenic patients. Postoperative complications were graded according to the Clavien–Dindo (CD) classification system.[24] Complications were defined as those that were CD grade II or higher.

### Screening for sarcopenia

Sarcopenia was assessed by calculating Skeletal Muscle Index using CT scan at L3 vertebrae. In this study CECT ABDOMEN which is used for the diagnosis of the gastrointestinal malignancy was used for calculating the SMI. No separate CECT ABDOMEN was done for calculating SMI. In this study patients were subjected for CT scan in 64 slice MDCT (Light speed VLT –XTE Gc medial system) and the cross-sectional images at the level of L3 vertebral body at which both transverse processes were visualized. The area of the muscle's psoas, quadratus lumborum, erector spinae muscles, transversus abdominis, internal and external obliques and rectus abdominis muscles were evaluated manually by the area measurement tool using RadiAnt DICOM viewer. The threshold range for skeletal muscle was -30 to +150 Hounsfield units. The skeletal muscle area was normalized for height to calculate the skeletal muscle index.



The skeletal muscle index is calculated as follows:-

| |
|---|
| Cross-sectional area of the total skeletal muscles at L3 (psoas, quadratus lumborum, erector spinae, transversus abdominis, internal and external obliques and rectus abdominis muscles) in $[cm]^2$ |
| Height $[m]^2$ |

Patients were categorized into sarcopenic and non-sarcopenic groups based on CT measurement of total skeletal muscle mass in cross sectional area at the level of L3. Based on EWGSOP2 (The European Working Group on Sarcopenia in Older People 2) recommendations, SMI < 55 $cm^2/m^2$ was considered the cutoff for men, compared to < 39 $cm^2$ for women.

### Statistical analysis

The presentation of the Categorical variables was done in the form of number and percentage (%). On the other hand, the quantitative data were presented as the means ± SD and as median with 25th and 75th percentiles (interquartile range). The following statistical tests were applied for the results:

1. The association of the variables which were quantitative in nature were analysed using Independent t test (for two groups) and ANOVA (for more than two groups).
2. The association of the variables which were qualitative in nature were analysed using Chi-Square test. If any cell had an expected value of less than 5 then Fisher's exact test was used.

The data entry was done in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver 25.0.For statistical significance, p value of less than 0.05 was considered statistically significant. Ethical approval was obtained from institutional ethical committee.

## RESULTS

Patient characteristics

Forty-one patients were included in the study and had a mean age of 60.66 ± 12.93years.

Among the 41 patients with diagnosis of gastric cancer; 18 patients (43.90 %) were diagnosed as sarcopenic and the remaining 23 patients (56.1%) based on EWGSOP2 (The European Working Group on Sarcopenia in Older People 2) recommendations. The mean age of patients with sarcopenia with gastric malignancy was 65.94 years and the mean age of patients without sarcopenia with gastric malignancy was 55.49 years The prevalence of sarcopenia was remarkably higher among patients more than 60 years of age. Clinicopathological features of the two groups are shown in Table 1.

Regarding gender, the proportion of men was higher in the sarcopenic group than women in the non-sarcopenic group (61.1% vs. 38.8 %). Of body weight and composition , mean body mass index (BMI) was lower in the sarcopenic group than in the nonsarcopenic group (19.64 ± 3.36 vs. 20.18± 3.38 kg/m $^2$). Nutritional parameters such as mean serum albumin was lower in the sarcopenic group than in the non sarcopenic group (sarcopenic, 3.05± .42g/dl vs. non-sarcopenic, 3.24± .42 g/dl). Mean skeletal muscle index (cm²/m²) in patients of gastric carcinoma in sarcopenic patients was 44.08±8.93cm²/m² while skeletal muscle index (cm²/m²) in patients of gastric carcinoma in non sarcopenic patients was 46.19±9.13cm²/m².

**Table 1: Clinicopathological features of sarcopenic and non-sarcopenic patients.**

| Clinicopathological features | Sarcopenic group(n=18) | Non Sarcopenic group(n=23) |
|---|---|---|
| Mean age(years) | 65.94 | 55.49 |
| Gender<br>Men<br>Women | 11(61.1%)<br>7(31.8%) | 12(52.17%)<br>11(47.82%) |
| BMI (kg/m $^2$) | 19.64 ± 3.36 | 20.18± 3.38 |
| Serum albumin(g/dl) | 3.05± .42 | 3.24± .42 |
| SMI(cm²/m²) | 46.19±9.13 | 46.19±9.13 |

**Table 2: Association of complications in operable cases in sarcopenic and non-sarcopenic patients.**

| GASTRIC CANCER(n=8) | | | |
|---|---|---|---|
| | Sarcopenic Group (n=3) | Non Sarcopenic Group (n=5) | P value |
| Complications | Frequency | Frequency | |
| No Complications | 1(33.33%) | 3(60%) | .07 |
| Total Complications(>=grade2) | 2(66.66%) | 2(40%) | |
| Grade 2 | 1(33.33%) | NIL | .03 |
| Grade 3 | 1(33.33%) | 1(20%) | |
| Grade 5 | NIL | 1(20%) | |

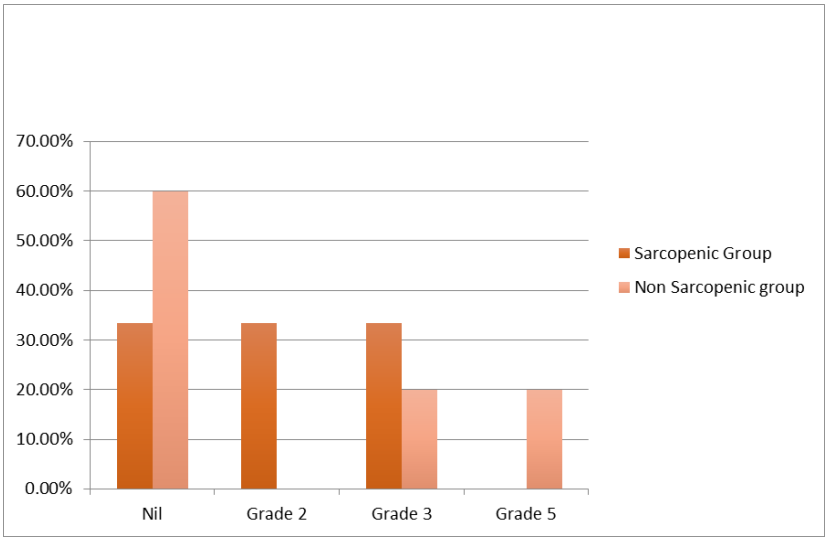



**Figure 2: Association of complications in operable cases in sarcopenic and non-sarcopenic patients.**

**Impact of sarcopenia on postoperative complications in operable cases**

Of 41 patients who were diagnosed with gastric cancer 8 patients were operable and they underwent gastrectomy. Out of these 8 patients, 3 patients were sarcopenic and 5 were non sarcopenic.5 patients developed postoperative complications. In patients without sarcopenia there were no complications in three (60%) patients followed by grade 3 complications in one (20%) patient followed by grade 5 complications in one (20%) patient according to

Clavien Dindo classification and in patients with sarcopenia there were grade 2 complications in three (60%) patients followed by no complications in two(40%) patients according to Clavien Dindo classification. Table and figure 2 shows the association of postoperative complications in operable cases in the two groups. Although there significant difference in the overall complication rate (sarcopenic, 66.66 %, vs. non-sarcopenic, 40 %; P = 0.03).

## DISCUSSION

Surgery remains the most common curative treatment for gastrointestinal cancers. In addition to lowering adherence to postoperative treatment and raising healthcare expenses, postoperative difficulties can worsen oncological outcomes by compromising healthy lifestyles.[25] In this regard, it is crucial to stratify surgical candidates based on their likelihood of experiencing postoperative problems; nevertheless, this process is still difficult.

Furthermore, with a rapidly aging population, it is imperative to comprehend the etiology of geriatric illnesses. Sarcopenia is a reduction in muscle mass and physical function that is primarily brought on by aging[5] and subsequently brought on by cancer.[6] It is a significant factor in frailty in older adults. Adverse postoperative outcomes following colorectal cancer resection.[12,13], pancreatic cancer[17], hepatocellular carcinoma[11,15], metastatic liver cancer[14], and perihilar cholangiocarcinoma[16] have all been linked to it in the past. In the current investigation, we showed that elderly patients with gastric cancer had a greater frequency of severe postoperative sequelae and a higher prevalence of sarcopenia prior to surgery. According to research by Mourtzakis and colleagues[26], there is a direct correlation between whole-body SM in cancer patients and the cross-sectional area of skeletal muscle at the level of the third lumbar vertebra. The current gold standard for determining total skeletal muscle mass is the assessment of the skeletal muscle index at L3 using CECT. The most common methods for predicting preoperative sarcopenia and examining the connection between sarcopenia and postoperative outcomes have been using computed tomography (CT) imaging. Studies, however, use different methodologies when assessing the skeletal muscle index and sarcopenia cutoff points. Cut-off points depend on the measurement technique and on the availability of reference studies and populations. Various studies have been used for assessing the sarcopenia by CT in various regions of the world and various cut offs have been devised by each of the study. In this study, cutoff introduced by EWGSOP2 (The European Working Group on Sarcopenia in Older People 2) which defines sarcopenia when Lumbar skeletal muscle index by CT imaging (3rd lumbar vertebra) in Men < 55 $cm^2/m^2$ and in Women < 39 $cm^2/m^2$was used. Sarcopenia in cancer is conceptionally similar to cancerous cachexia, which is associated with cancer progression and sequential dystrophy. Fearon et al.[27] classified cancerous cachexia as precachexia, cachexia, and refractory cachexia, with the presence of sarcopenia as a key component of cachexia. In addition, involuntary weight loss and low BMI are frequently the first symptoms observed in cancer patients[28]; these symptoms place them in the first phase of cachexia.[27] In fact, preoperative sarcopenia was associated with lower BMI in previous studies[11–14, 16] as well as in the current study,; it might be associated with more advanced disease stage and decreased food intake in our study. In contrast, serum albumin, routinely monitored as a nutritional parameter, was lower in the sarcopenic and non-sarcopenic groups. Although few studies have demonstrated a relationship between preoperative sarcopenia and serum albumin levels, we speculated that decreases in serum albumin are observed as patients move closer to the stage of refractory cachexia and that this decrease may not be observed early in cachexia. Several studies have reported that sarcopenia is independently associated with postoperative complications (CD grade IIa or higher)[14,16,17], consistent with our findings in this study. Preoperative intervention is important for treating sarcopenia and preventing severe postoperative complications. The current study has several limitations. This was a single-center prospective observational study and the sample size was small. A validation study with large sample size will be necessary to confirm the impact of preoperative sarcopenia on postoperative complications. In conclusion, sarcopenia, as assessed by the EWGSOP 2 recommendations, is prevalent among gastric cancer patients. Sarcopenia is associated with the development of severe postoperative complications.

### Compliance with ethical standards

Ethical standards All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1964 and later versions. Informed consent was obtained from all patients for inclusion in the study.

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**Conflict of interest:** We declare that we have no conflicts of interest

Authors' Biography

## REFERENCES

1. Rosenberg IH. Sarcopenia: origins and clinical relevance. J Nutr., 1997; 127: 990S–1S.
2. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European Working Group on Sarcopenia in Older People. Age Ageing., 2010; 39: 412–23.
3. Chen LK, Liu LK, Woo J, Assantachai P, Auyeung TW, Bahyah KS, et al. Sarcopenia in Asia: consensus report of the Asian Working Group for

Sarcopenia. J Am Med Dir Assoc, 2014; 15: 95–101.
4. Yoshida D, Suzuki T, Shimada H, Park H, Makizako H, Doi T, et al. Using two different algorithms to determine the prevalence of sarcopenia. Geriatr Gerontol Int., 2014; 14: 46–51.
5. Baumgartner RN, Koehler KM, Gallagher D, Romero L, Heymsfield SB, Ross RR, et al. Epidemiology of sarcopenia among the elderly in New Mexico. Am J Epidemiol, 1998; 147: 75 5–63.
6. Muscaritoli M, Anker SD, Argiles J, Aversa Z, Bauer JM, Biolo G, et al. Consensus definition of sarcopenia, cachexia and pre-cachexia: joint document elaborated by Special Interest Groups SIG) ''cachexia-anorexia in chronic wasting diseases'' and''nutrition in geriatrics''. Clin Nutr., 2010; 29: 154–9.
7. Rofe AM, Bourgeois CS, Coyle P, Taylor A, Abdi EA. Altered insulin response to glucose in weight-losing cancer patients. Anticancer Res., 1994; 14: 647–50.
8. Laviano A, Mequid MM, Inui A, Muscaritoli M, Rossi-Fanellli F. Therapy insight: cancer anorexia-cachexia syndrome—when all you can eat is yourself. Nat Clin Pract Oncol, 2005; 2: 158–65.
9. Scott D, Blizzard L, Fell J, Giles G, Jones G. Associations between dietary nutrient intake and muscle mass and strength in community-dwelling older adults: the Tasmanian Older Adult Cohort Study. J Am Geriatr Soc., 2010; 58: 2129–34.
10. Valenzuela RE, Ponce JA, Morales-Figueroa GG, Muro KA, Carreon VR, Aleman-Mateo H. Insufficient amounts and inadequate distribution of dietary protein intake in apparently healthy older adults in a developing country: implications for dietary strategies to prevent sarcopenia. Clin Interv Aging, 2013; 8: 1143–8.
11. Voron T, Tselikas L, Pietrasz D, Pigneur F, Laurent A, Compagnon P, et al. Sarcopenia impacts on short- and long-term results of hepatectomy for hepatocellular carcinoma. Ann Surg, 2014; 00: 1–11.
12. Lieffers JR, Bathe OF, Fassbender K, Winget M, Baracos VE. Sarcopenia is associated with postoperative infection and delayed recovery from colorectal cancer resection surgery. Br J Cancer, 2012; 107: 931–6.
13. Peng PD, van Vledder MG, Tsai S, de Jong MC, Makary M, Ng J, et al. Sarcopenia negatively impacts short-term outcomes in patients undergoing hepatic resection for colorectal liver metastasis. HPB (Oxf), 2011; 13: 439–46.
14. Peng PD, van Vledder MG, Tsai S, de Jong MC, Makary M, Ng J, et al. Sarcopenia negatively impacts short-term outcomes in patients undergoing hepatic resection for colorectal liver metastasis. HPB (Oxf), 2011; 13: 439–46.
15. Valero V, Amini N, Spolverato G, Weiss MJ, Hirose K, Dagher NM, et al. Sarcopenia adversely impacts postoperative complications following resection or transplantation in patients with primary liver tumors. J Gastrointest Surg, 2015; 19: 272–81.
16. Otsuji H, Yokoyama Y, Ebata T, Igami T, Sugawara G, Mizuno T, et al. Preoperative sarcopenia negatively impacts postoperative outcomes following major hepatectomy with extrahepatic bile duct resection. World J Surg, 2015. doi:10.1007/s00268-0152988-6.
17. Joglekar S, Asghar A, Mott SL, Johnson BE, Button AM, Clark E, et al. Sarcopenia is an independent predictor of complications following pancreatectomy for adenocarcinoma. J Surg Oncol, 2015; 111: 771–5.
18. Tan BH, Birdsell LA, Martin L, Baracos VE, Fearon KC. Sar-copenia in an overweight or obese patient is an adverse prognostic factor in pancreatic cancer. Clin Cancer Res., 2009; 15: 6973–9.
19. Harimoto N, Shirabe K, Yamashita YI, Ikegami T, Yoshizumi T, Soejima Y, et al. Sarcopenia as a predictor of prognosis in patients following hepatectomy for hepatocellular carcinoma. Br J Surg, 2013; 100: 1523–30.
20. Miyamoto Y, Baba Y, Sakamoto Y, Ohuchi M, Tokunaga R, Kurashige J, et al. Sarcopenia is a negative prognostic factor after curative resection of colorectal cancer. Ann Surg Oncol. 2015. doi:10.1245/s10434-014-4281-6.
21. Mir O, Coriat R, Blanchet B, Durand JP, Boudou-Rouquette P, Michels J, et al. Sarcopenia predicts early dose-limiting toxicities and pharmacokinetics of sorafenib in patients with hepatocellular carcinoma. PLoS One, 2012; 7: e37563.
22. Prado CM, Baracos VE, McCarger LJ, Reiman T, Mourtzakis M, Tonkin K, et al. Sarcopenia as a determinant of chemotherapy stoxicity and time to tumor progression in metastatic breast cancer patients receiving capecitabine treatment. Clin Cancer Res., 2009; 15: 2920–6.
23. Tan BH, Brammer K, Randhawa N, Welch NT, Parsons SL, James EJ, et al. Sarcopenia is associated with toxicity in patients undergoing neo-adjuvant chemotherapy for oesophago-gastriccancer. Eur J Surg Oncol, 2015; 41: 333–8.
24. Clavien OA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, et al. Ann Surg, 2009; 250: 187–96.
25. Tokunaga M, Tanizawa Y, Bando E, Kawamura T, Terashima M. Poor survival rate in patients with postoperative intra-abdominal infectious complications following curative gastrectomy for gastric cancer. Ann Surg Oncol, 2013; 20: 1575–83.
26. Mourtzakis M, Prado CM, Lieffers JR, Reiman T, McCargar LJ, Baracos VE. A practical and precise approach to quantification ofbody composition in cancer patients using computed tomography images acquired during routine care. Appl Physiol Nutr Metab, 2008; 33: 997–1006.
27. Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, et al. Definition and classification

of cancer cachexia: an international consensus. Lancet Oncol, 2011; 12: 489–95.

28. Dewys WD, Begg C, Lavin PT, Band PR, Bennett JM, Bertino JR, et al. Prognostic effect of weight loss prior to chemotherapy in cancer patients. Eastern Cooperative Oncology Group. Am J. Med., 1980; 69: 491–7.