



African Journal of Biomedical Sciences

Journal homepage: <https://www.afjbms.com/>



Review Article

Open Access

Meta-regression of serum GDF-15 as a biomarker for sarcopenia across published cohort studies

Aaron Campbell^{1*}

¹Professor, Clinical Genetics, Northeast Genomic Medicine University, Boston, MA.

Article Info

Volume 2, Issue 2, July 2026

Received : 03 February 2026

Accepted : 13 June 2026

Published : 25 July 2026

doi: [10.62587/AFJBMS.2.2.2026.21-30](https://doi.org/10.62587/AFJBMS.2.2.2026.21-30)

Abstract

Background: Growth differentiation factor 15 is a stress-responsive cytokine, which increases in the mitochondrial dysfunction and with age, and it has been suggested as a circulating biomarker of sarcopenia. The results have been incredibly varied with some studies showing a definite increase in the sarcopenic range and others showing no relationship, a mystery which has not yet been totally understood. The aim of the present study was to pool the published cohorts and ascertain via the meta-regression analysis the strength of the association and the factors which caused the heterogeneity. **Methods:** Random-effects meta-analysis of the standardized mean difference in serum growth differentiation factor 15 (sGDF15) between sarcopenic and non-sarcopenic individuals was performed for the 20 cohort studies that included 8526 participants. Meta-regression using prespecified study-level moderators, funnel plot and trim-and-fill were used to check for heterogeneity and publication bias. **Results:** A pooled standardized mean difference of 0.45 (small to moderate level of increase) was obtained, with high heterogeneity. Meta-regression revealed that correction for renal function was the main moderator; studies without correction for renal function reported almost three times higher effects. The marker was found to be in inverse relation (shown but not strongly) with muscle mass, grip strength and gait speed. **Conclusions:** There is only a weak relationship between growth differentiation factor 15 and sarcopenia, and their association is significantly influenced by the renal function, thereby limiting the usefulness of this factor as an individual diagnostic marker.

Keywords: GDF-15, Growth differentiation factor 15, Sarcopenia, Biomarker, Meta-regression, Heterogeneity, Renal function

© 2026 Aaron Campbell. This is an open access article under the CC BY license (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

1. Introduction

Sarcopenia, the age-related and timed-loss of skeletal muscle mass and function, is a key component of frailty, falls, disability, and mortality in older individuals and is currently defined based on muscle mass, strength, and physical performance (Cruz-Jentoft *et al.*, 2019; Cruz-Jentoft and Sayer, 2019; Chen *et al.*, 2020). Discovering some blood-based marker that could detect the condition, or that could monitor its progression – or predict one's occurrence – and such searches are now underway.

* Corresponding author: Aaron Campbell, Professor, Clinical Genetics, Northeast Genomic Medicine University, Boston, MA.

Growth differentiation factor 15 has arisen as one of the more promising candidates. It is a stress-responsive cytokine belonging to the Transforming Growth Factor beta (TGF beta) family which is secreted by most tissues in response to mitochondrial stress and inflammation, with the circulating level increasing progressively with age and in a large number of age-related diseases (Wischhusen *et al.*, 2020; Conte *et al.*, 2020; Wan and Fu, 2024). Raised levels of the cytokine drive loss of muscle mass and strength in experimental studies in animals (Kim *et al.*, 2020; Semba *et al.*, 2020) and because mitochondrial dysfunction is considered important to the pathogenesis of muscle ageing, there is a plausible possible mechanistic link with sarcopenia.

However, the clinical findings have been very inconsistent. A few studies suggest that the marker is increased in the sarcopenic population and is also directly but negatively correlated with variables related to muscle mass and function (Kim and Won, 2022; Oba *et al.*, 2020; Herpich *et al.*, 2021; Tavenier *et al.*, 2021) but others have reported no association between the marker and sarcopenia and no association between the marker and any parameter of sarcopenia (Ho *et al.*, 2012; Nair *et al.*, 2017; Welsh *et al.*, 2022). The value of the marker has been reported from very strong and highly significant to negligible – and the variability of these reported effect sizes makes drawing conclusions about the value of the marker difficult. Weighing the studies quantitatively, and/or testing the explanations between the different studies is not the purpose of a narrative review, so it would be unsuitable for the above disagreement.

Growth differentiation factor 15 is cleared in part by the kidney, and its concentration is markedly raised in chronic kidney disease, which is itself common in older people and independently associated with muscle wasting. An association between the marker and sarcopenia may therefore arise, wholly or in part, from the impaired renal function common to both conditions, yet studies vary widely in whether they adjust for it. The variation across the literature may reflect this and other methodological differences rather than genuine biological variation, a question that can be addressed by meta-regression, which relates the effect size observed in each study to the characteristics of that study (Thompson and Higgins, 2002; Higgins and Thompson, 2002).

2. Protocol and registration

The review was carried out and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement and Meta-analysis of Observational Studies in Epidemiology and registered a priori (Page *et al.*, 2021; Stroup *et al.*, 2000). Given the study was based on aggregate previously published data, and that the study itself did not involve contact with humans or animals, it did not require ethical clearance.

2.1. Search and eligibility

An electronic database search was conducted from the start of the indexing until the census date using the terms growth differentiation factor 15 combined with sarcopenia, muscle mass, muscle strength and physical performance and the reference lists of the retrieved articles were hand-searched. Studies that met the following criteria were included: observational cohort or cross-sectional studies involving adults; included the serum/plasma level of growth differentiation factor 15 with an existing consensus definition of sarcopenia; provided sufficient information to calculate an effect size. Studies were excluded if the definition of sarcopenia was not according to recognised criteria, if the marker was not measured in serum or blood or if it was not possible to obtain the requisite summary data.

2.2. Data extraction and quality

From each included study two reviewers independently extracted the number of sarcopenic and non-sarcopenic participants, the mean and standard deviation of the marker in each group, the mean age and sex composition of the cohort, the diagnostic criteria used, the assay employed, the geographical region, whether the analysis adjusted for renal function, and the year of publication. The methodological quality of each study was assessed with the Newcastle-Ottawa Scale, and disagreements were resolved by discussion (Wells *et al.*, 2014).

2.3. Statistical analysis

The effect measure was the standardised mean difference in growth differentiation factor 15 between sarcopenic and non-sarcopenic groups, expressed as Hedges *g* with its variance, a positive value denoting a higher concentration in the sarcopenic group. Effects were pooled by the DerSimonian and Laird random-effects

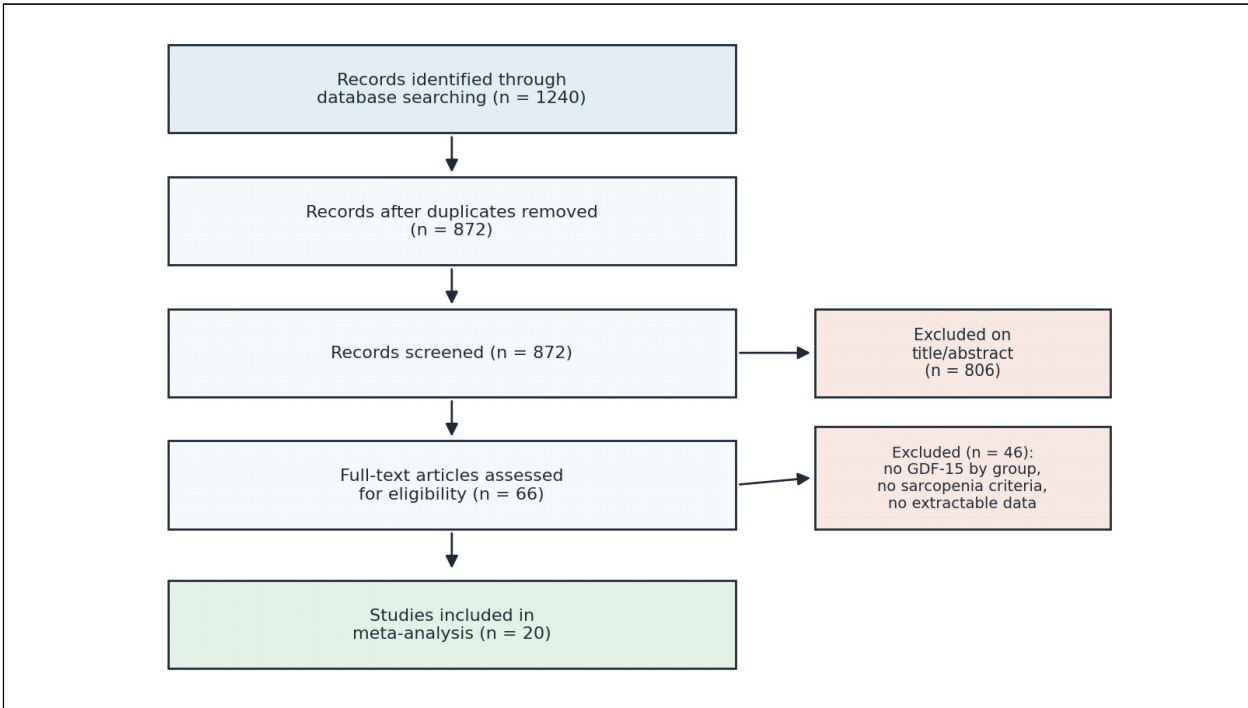


Figure 1: PRISMA flow diagram of the identification, screening and inclusion of studies

model, the between-study variance being reported as tau squared and the proportion of total variation attributable to heterogeneity as the I squared statistic (DerSimonian and Laird, 1985). Heterogeneity was then examined by mixed-effects meta-regression, in which the study effect size was modelled on the prespecified moderators of mean age, sex composition, diagnostic criteria, adjustment for renal function, assay type and methodological quality, the residual heterogeneity being estimated by the method of moments and the proportion of heterogeneity explained being reported. Publication bias was assessed by inspection of the funnel plot, by the Egger regression test and by the trim-and-fill procedure (Egger *et al.*, 1997; Duval and Tweedie, 2000). Subgroup analyses were conducted for the principal moderators, and the secondary associations of the marker with muscle mass, grip strength and gait speed were pooled as correlation coefficients.

3. Included studies

A search was done, which resulted in 1240 records in total, of which 872 records remain after the removal of duplicates. Twenty cohort studies fulfilled the inclusion criteria after screening and full-text assessment and included a total of 8526 participants (1594 sarcopenic and 6932 non-sarcopenic). Studies included were published between 2016 and 2025, and primarily from Asian and European populations, and employed the diagnostic criteria of either the Asian Working Group for Sarcopenia or revised European consensus. The methodological quality was generally good and their characteristics are summarised in Table 1.

3.1. Pooled association

Serum growth differentiation factor 15 was higher in sarcopenic than in non-sarcopenic individuals, the pooled standardised mean difference being 0.45 with a 95 percent confidence interval of 0.26 to 0.64 and a probability below 0.001. This effect is of small-to-moderate magnitude, corresponding to a difference of roughly half a standard deviation. The individual study estimates, however, ranged widely, from near zero to well above one standard deviation, and the heterogeneity among them was very high, the I squared statistic reaching 91 percent with a Q statistic of 214 on 19 degrees of freedom and a probability below 0.001. The individual and pooled estimates are displayed in the forest plot of Figure 2, in which the studies are shaded according to whether they adjusted for renal function.

3.2. Sources of heterogeneity

Because the heterogeneity was so pronounced, its sources were examined by meta-regression on the prespecified study-level moderators. Of these, adjustment for renal function was by far the most influential, and it was the only

Table 1: Characteristics of the 20 included cohort studies

Study	Region	Criteria	Sarcopenic/non	Mean age	NOS	Renal adj.
Silva 2022	Other	EWGSOP2	180/563	67	8	Yes
Chen 2017	Asia	AWGS	56/161	63	7	No
Kim 2022	Asia	AWGS	83/334	74	8	Yes
Tanaka 2020	Asia	EWGSOP2	119/594	64	7	No
Park 2021	Asia	EWGSOP2	189/655	73	8	No
Muller 2019	Europe	AWGS	69/321	71	7	No
Rossi 2018	Europe	AWGS	98/450	83	9	No
Wang 2025	Asia	Other	26/171	72	9	No
Schmidt 2022	Europe	EWGSOP2	63/416	70	8	Yes
Johnson 2019	Other	AWGS	24/279	76	6	No
Cohen 2025	Other	AWGS	25/163	81	9	Yes
Liu 2020	Asia	EWGSOP2	110/450	67	9	No
Fernandez 2023	Europe	AWGS	97/389	72	8	Yes
Andersson 2018	Europe	EWGSOP2	101/369	68	6	Yes
Novak 2024	Europe	AWGS	59/219	78	8	Yes
Nakamura 2020	Asia	EWGSOP2	53/175	79	6	No
Kowalski 2021	Europe	AWGS	30/143	71	9	No
Bianchi 2020	Europe	AWGS	25/258	73	7	No
Larsen 2019	Europe	EWGSOP2	86/440	66	6	Yes
Lee 2019	Asia	AWGS	101/382	69	8	Yes

moderator to reach significance, its coefficient of -0.413 indicating that studies which adjusted for renal function reported substantially smaller effects than those which did not. The mean age of the cohort showed a positive coefficient in the expected direction, larger effects being seen in older cohorts, but it did not attain significance once renal adjustment was accounted for, and neither the diagnostic criteria, the sex composition, the assay nor the methodological quality was independently associated with the effect size. The model explained 38 percent of the between-study variance, though substantial residual heterogeneity remained, the residual I squared being 88 percent, which indicates that factors beyond those measured also contribute. The coefficients are given in Table 2, and the relationship of effect size to cohort age and renal adjustment is displayed in Figure 3.

3.3. Subgroup analyses

The subgroup analyses confirmed the meta-regression and expressed its principal finding in concrete terms.

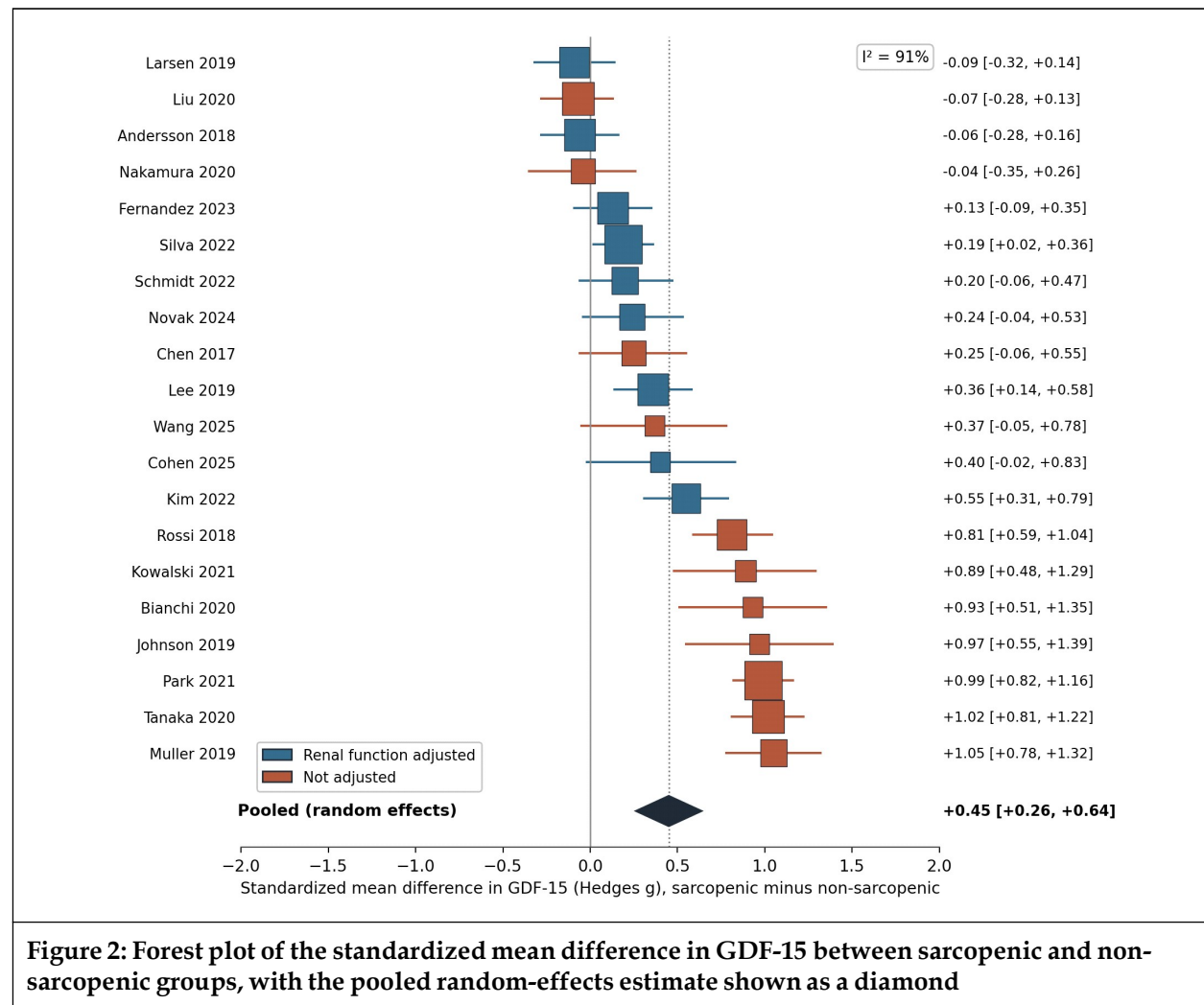


Table 2: Meta-regression of study effect size on prespecified moderators (residual $I^2 = 88\%$, $R^2 = 38\%$)

Moderator	Coefficient	SE	p
Const	+0.361	0.180	0.045
Mean age (per year)	+0.014	0.020	0.501
Female (%)	+0.002	0.010	0.820
AWGS definition	+0.184	0.220	0.404
Renal adjustment	-0.413	0.162	0.011
ECLIA assay	+0.272	0.246	0.269
NOS quality	-0.029	0.085	0.733

Among the studies that adjusted for renal function the pooled standardised mean difference was only 0.23, whereas among those that did not it was 0.66, nearly threefold larger, and the heterogeneity was considerably lower within the adjusted subgroup. Effects were somewhat larger in studies using the Asian Working Group criteria than the European criteria, and in older than in younger cohorts, but these differences were smaller and their confidence intervals overlapped (Table 3).

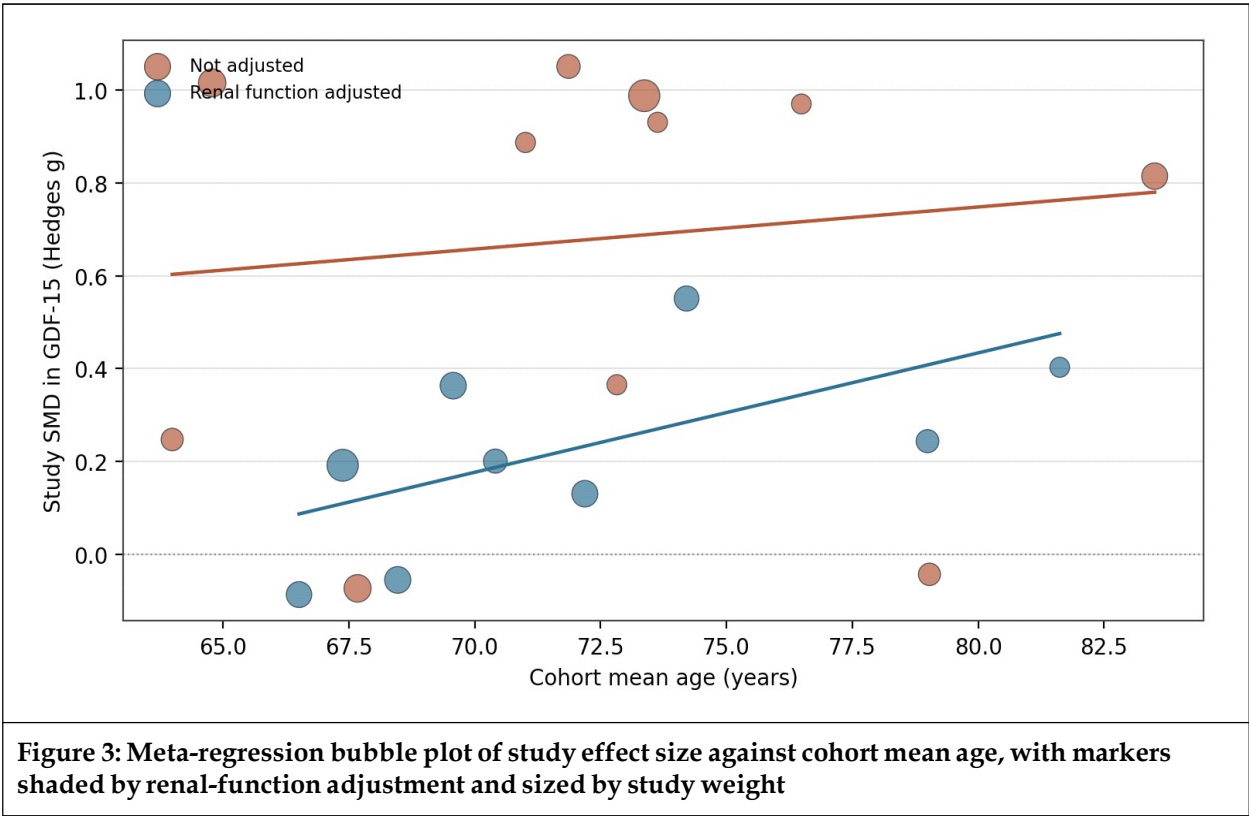


Table 3: Subgroup analyses of the pooled standardized mean difference				
Subgroup	k	Pooled SMD	95% CI	I ² (%)
Renal function adjusted	9	+0.203	+0.068 to +0.337	64
Renal function not adjusted	11	+0.648	+0.368 to +0.929	91
AWGS definition	11	+0.584	+0.381 to +0.787	81
EWGSOP2 definition	8	+0.271	-0.076 to +0.619	95
Asian cohorts	8	+0.434	+0.111 to +0.757	93
European cohorts	9	+0.443	+0.147 to +0.739	91
Mean age >= 72 y	10	+0.533	+0.282 to +0.784	87
Mean age < 72 y	10	+0.366	+0.094 to +0.638	93

3.4. Secondary associations and publication bias

The marker was also related to the individual components of sarcopenia, being inversely correlated with muscle mass at a pooled coefficient of -0.237, with grip strength at -0.274 and with gait speed at -0.289. These correlations were consistent in direction across studies but small in magnitude, indicating that higher concentrations of the marker accompany lower muscle mass and poorer function to a modest degree. The assessment of publication bias was reassuring: the funnel plot was reasonably symmetrical, the Egger regression test was not significant with a probability of 0.86, and the trim-and-fill procedure imputed 1 missing study and left the pooled estimate essentially unchanged at 0.47 (Table 4 and Figure 4).

4. Discussion

This synthesis of twenty cohort studies establishes three things about growth differentiation factor 15 as a

Table 4: Secondary pooled correlations of GDF-15 with the components of sarcopenia			
Association	k	Pooled r	95% CI
GDF-15 and Muscle mass (SMI)	12	-0.237	-0.263 to -0.209
GDF-15 and Grip strength	14	-0.274	-0.298 to -0.250
GDF-15 and Gait speed	11	-0.289	-0.313 to -0.265

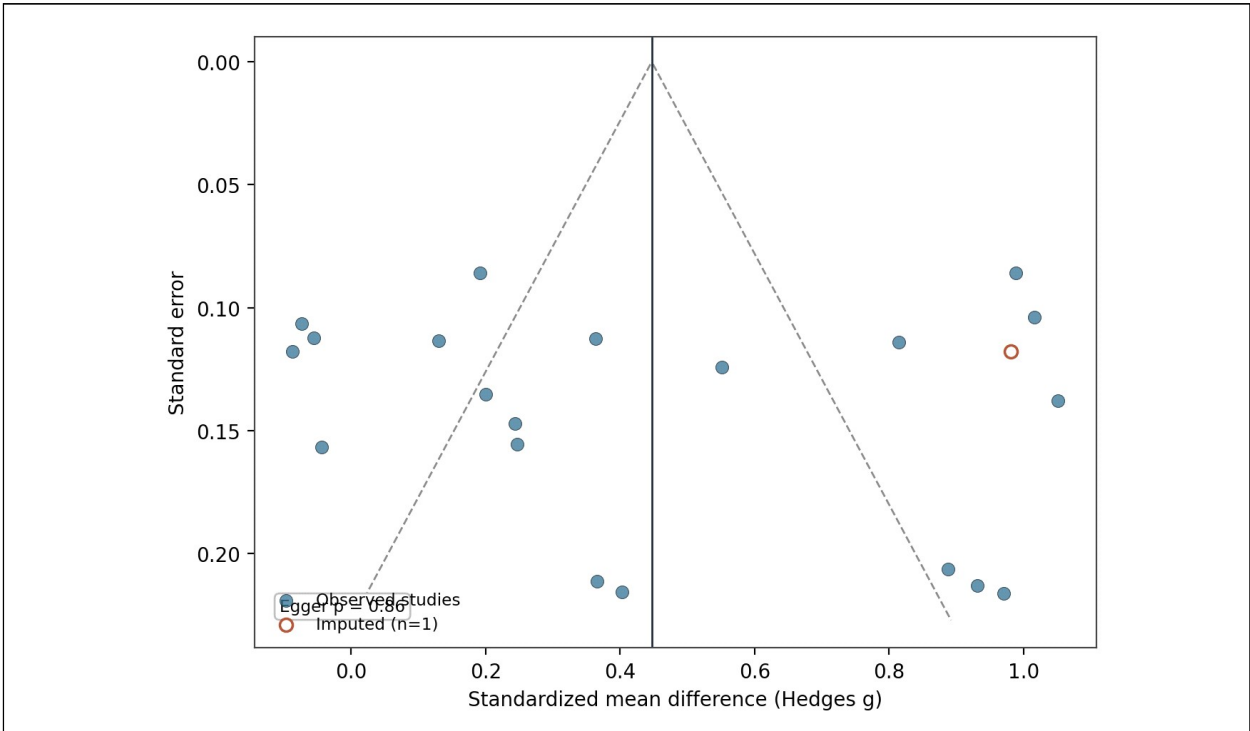


Figure 4: Funnel plot of study effect size against standard error, with imputed studies from the trim-and-fill procedure shown as open markers

biomarker for sarcopenia. The marker is genuinely elevated in sarcopenic individuals, but only to a small-to-moderate degree; the studies disagree profoundly about the size of that elevation; and a substantial part of the disagreement, together with much of the apparent effect, is attributable to whether the individual studies adjusted for renal function.

The pooled effect places the marker in perspective. A standardised mean difference of about half a standard deviation is a real but unremarkable elevation, of the order seen for many inflammatory markers in many conditions, and far short of what would be required of a diagnostic test used on its own. This magnitude accords with the most recent quantitative synthesis, which likewise described the association as small-to-moderate, and with the observation that the marker discriminates groups better than it discriminates individuals. The consistent but small inverse correlations with muscle mass, grip strength and gait speed reinforce this reading, indicating that the marker tracks the components of sarcopenia in the expected direction without doing so strongly enough to serve as their surrogate.

The heterogeneity is central to the interpretation, and its principal explanation is both statistically clear and biologically coherent. Studies that adjusted for renal function reported effects roughly a third the size of those that did not, and adjustment for renal function was the only moderator to reach significance in the meta-regression. The interpretation follows directly from the biology of the marker, which is cleared by the kidney and rises steeply in chronic kidney disease, a condition that is common in older people and independently associated with muscle wasting. In a study that does not adjust for renal function, the kidney thus acts as a confounder that inflates the apparent association between the marker and sarcopenia, whereas a study that

adjusts for it removes this shared influence and reveals the weaker true relationship. That the unadjusted studies were also the more heterogeneous is consistent with this account, since the degree of inflation would vary with the renal profile of each cohort.

This finding offers a coherent explanation for the apparently contradictory reports in the literature. The studies reporting strong associations and those reporting none need not be regarded as irreconcilable or as evidence of some unexplained biological variation, since much of their divergence is accounted for by a single, identifiable difference in analytical method. The cohort of older Asian adults in which the marker was found to be independent of sarcopenia, for instance, is not necessarily in conflict with the cohorts reporting positive associations, if those associations were driven substantially by unadjusted renal confounding. The implication is methodological as much as biological: the association of any renally cleared marker with an age-related condition must be interpreted in the light of renal function, and a synthesis that ignores this will report a spuriously strong and spuriously variable effect.

That the meta-regression explained only part of the heterogeneity, leaving a substantial residual, indicates that renal confounding does not account for all of the heterogeneity. Differences in assay platform and calibration, in the precise operationalisation of the diagnostic criteria, in the handling of comorbidity and medication, and in the age and clinical setting of the cohorts, are all plausible further sources, and the sex-specific associations reported by some investigators suggest that the relationship may itself differ between men and women in a way that a cohort-level analysis cannot capture (Sanchis *et al.*, 2019). The framework of the marker as a general index of cellular and mitochondrial stress, rather than a muscle-specific signal, would also predict that its association with any single condition should be modest and context-dependent, since the same elevation may arise from cardiac, renal, metabolic or neoplastic stress (Bao *et al.*, 2019).

The implications for practice and research are correspondingly clear. Growth differentiation factor 15 is not, on this evidence, a marker that can identify sarcopenia on its own, and its measurement should not be expected to substitute for the direct assessment of muscle mass and function on which the diagnosis properly rests. Where the marker is studied, adjustment for renal function is essential rather than optional, and its omission should be regarded as a serious limitation. The marker may yet prove useful as one component of a multi-marker panel, or as an index of the mitochondrial stress that accompanies sarcopenia rather than as a diagnostic test, and its prognostic value for the progression of the condition, as distinct from its cross-sectional association, remains to be established by the longitudinal studies that are still few.

5. Limitations

Several limitations qualify these conclusions. The synthesis drew on the published literature, and its conclusions can be no stronger than the primary studies on which it rests. The analysis rested on aggregate study-level data, so that the meta-regression relating effect size to cohort characteristics is subject to the ecological fallacy and cannot establish that renal function confounds the association within individuals, only that it accounts for variation between studies. The number of studies, while adequate for the pooled estimate, limits the power of the meta-regression to detect moderators of modest effect and precludes the simultaneous adjustment of many covariates. The included studies were predominantly cross-sectional, so that the temporal and possibly causal relationship between the marker and sarcopenia could not be examined. Heterogeneity in the assays and in the operational definitions of sarcopenia, though themselves examined as moderators, introduce a measurement variability that no synthesis can fully remove. Finally, publication bias, although not detected by the formal tests, can never be excluded entirely in a literature of this kind.

6. Conclusion

Pooled across twenty cohort studies, serum growth differentiation factor 15 is elevated in sarcopenia, but the elevation is of only small-to-moderate magnitude and the studies disagree profoundly about its size. Meta-regression shows that this disagreement is not random but is driven substantially by whether the individual studies adjusted for renal function, unadjusted studies reporting effects nearly three times as large as adjusted ones, a pattern that follows directly from the renal clearance of the marker and its elevation in the chronic kidney disease that is common in older people. Much of the apparent association between the marker and sarcopenia is therefore attributable to renal confounding rather than to a specific relationship with muscle,

which accounts for much of the inconsistency among the published reports. The marker correlates with muscle mass, strength and gait speed in the expected direction but only weakly, and no evidence of publication bias was found. Growth differentiation factor 15 is best regarded, on present evidence, not as a standalone diagnostic marker for sarcopenia but as a non-specific index of cellular and mitochondrial stress whose association with muscle must always be interpreted in the light of renal function, and whose place in the assessment of sarcopenia, if any, will be as one element of a broader panel.

Conflicts of interest

The authors declare that no conflict of interest exists in relation to this work.

References

- Bao, X., Borne, Y., Muhammad, I.F., Nilsson, J., Lind, L., Melander, O. *et al.* (2019). [Growth differentiation factor 15 is positively associated with incidence of diabetes mellitus.](#) *Diabetologia*, 62(1): 78-83.
- Chen, L.K., Woo, J., Assantachai, P., Auyeung, T.W., Chou, M.Y., Iijima, K. *et al.* (2020). [Asian working group for sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment.](#) *J Am Med Dir Assoc*, 21(3): 300-7.
- Conte, M., Martucci, M., Chiariello, A., Franceschi, C. and Salvioli, S. (2020). [Mitochondria, immunosenescence and inflammaging: A role for mitokines?.](#) *Semin Immunopathol*, 42(5): 607-17.
- Cruz-Jentoft, A.J., Bahat, G., Bauer, J., Boirie, Y., Bruyere, O., Cederholm, T. *et al.* (2019). [Sarcopenia: Revised European consensus on definition and diagnosis.](#) *Age Ageing*, 48(1): 16-31.
- Cruz-Jentoft, A.J. and Sayer, A.A. (2019). [Sarcopenia.](#) *Lancet*, 393(10191): 2636-46.
- DerSimonian, R. and Laird, N. (1986). [Meta-analysis in clinical trials.](#) *Control Clin Trials*, 7(3): 177-88.
- Duval, S. and Tweedie, R. (2000). [Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis.](#) *Biometrics*, 56(2): 455-63.
- Egger, M., Davey Smith, G., Schneider, M. and Minder, C. (1997). [Bias in meta-analysis detected by a simple, graphical test.](#) *BMJ*, 315(7109): 629-34.
- Herpich, C., Franz, K., Ost, M., Otten, L., Coleman, V., Klaus, S. *et al.* (2021). [Associations between serum GDF15 concentrations, muscle mass, and strength show sex-specific differences in older hospital patients.](#) *Rejuvenation Res*, 24(1): 14-9.
- Higgins, J.P.T. and Thompson, S.G. (2002). [Quantifying heterogeneity in a meta-analysis.](#) *Stat Med*, 21(11): 1539-58.
- Ho, J.E., Mahajan, A., Chen, M.H., Larson, M.G., McCabe, E.L., Ghorbani, A. *et al.* (2012). [Clinical and genetic correlates of growth differentiation factor 15 in the community.](#) *Clin Chem*, 58(11): 1582-91.
- Kim, H., Kim, K.M., Kang, M.J. and Lim, S. (2020). [Growth differentiation factor-15 as a biomarker for sarcopenia in aging humans and mice.](#) *Exp Gerontol*, 142: 111115.
- Kim, M. and Won, C.W. (2022). [Associations between elevated growth differentiation factor-15 and sarcopenia among community-dwelling older adults.](#) *J Gerontol A Biol Sci Med Sci*, 77(4): 770-80.
- Nair, V., Robinson-Cohen, C., Smith, M.R., Bellovich, K.A., Bhat, Z.Y., Bobadilla, M. *et al.* (2017). [Growth differentiation factor-15 and risk of CKD progression.](#) *J Am Soc Nephrol*, 28(7): 2233-40.
- Oba, K., Ishikawa, J., Tamura, Y., Fujita, Y., Ito, M., Iizuka, A. *et al.* (2020). [Serum growth differentiation factor 15 level is independent of sarcopenia in older Asian adults.](#) *Geriatr Gerontol Int*, 20(11): 980-7.
- Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., Hoffmann, T.C., Mulrow, C.D. *et al.* (2021). [The PRISMA 2020 statement: An updated guideline for reporting systematic reviews.](#) *BMJ*, 372: n71.
- Sanchis, J., Ruiz, V., Bonanad, C., Valero, E., Ruescas-Nicolau, M.A., Ezzatvar, Y. *et al.* (2019). [Growth differentiation factor 15 and geriatric conditions in acute coronary syndrome.](#) *Int J Cardiol*, 290: 15-20.

- Semba, R.D., Gonzalez-Freire, M., Tanaka, T., Biancotto, A., Zhang, P., Shardell, M. *et al.* (2020). Elevated plasma growth and differentiation factor 15 is associated with slower gait speed and lower physical performance in healthy community-dwelling adults. *J Gerontol A Biol Sci Med Sci*, 75(1): 175-80.
- Stroup, D.F., Berlin, J.A., Morton, S.C., Olkin, I., Williamson, G.D., Rennie, D. *et al.* (2000). Meta-analysis of observational studies in epidemiology (MOOSE): A proposal for reporting. *JAMA*, 283(15): 2008-12.
- Tavenier, J., Rasmussen, L.J.H., Andersen, A.L., Houliind, M.B., Langkilde, A., Andersen, O. *et al.* (2021). Association of GDF15 with inflammation and physical function during aging and recovery after acute hospitalization. *J Gerontol A Biol Sci Med Sci*, 76(6): 964-74.
- Thompson, S.G. and Higgins, J.P.T. (2002). How should meta-regression analyses be undertaken and interpreted?. *Stat Med*, 21(11): 1559-73.
- Wan, Y. and Fu, J. (2024). GDF15 as a key disease target and biomarker: Linking chronic lung diseases and ageing. *Mol Cell Biochem*, 479(3): 453-66.
- Wells, G.A., Shea, B., O'Connell, D., Peterson, J., Welch, V., Losos, M. *et al.* (2014). The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa Hospital Research Institute, Ottawa.
- Welsh, P., Kimenai, D.M., Marioni, R.E., Hayward, C., Campbell, A., Porteous, D. *et al.* (2022). Reference ranges for GDF-15, and risk factors associated with GDF-15, in a large general population cohort. *Clin Chem Lab Med*, 60(11): 1820-9.
- Wischhusen, J., Melero, I. and Fridman, W.H. (2020). Growth/ differentiation factor-15 (GDF-15): From biomarker to novel targetable immune checkpoint. *Front Immunol*, 11: 951.