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Glycaemic and Cardiometabolic Effects of Oral Semaglutide in Patients Aged ≥65 Years with Type 2 Diabetes

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Abstract

Background: Older patients with type 2 diabetes mellitus (T2DM) are often undertreated because of concerns regarding hypoglycaemia and clinical heterogeneity. Although the evidence base for oral semaglutide is growing, data specifically in older adults remain relatively limited, particularly regarding long-term effectiveness and tolerability in routine practice. Methods: This observational study included 81 patients aged ≥65 years with T2DM treated with oral semaglutide for 12 months. Changes in glycaemic, anthropometric and cardiometabolic parameters were evaluated. The primary endpoint was the achievement of HbA1c < 7% at 12 months. Multivariable logistic regression was performed to identify baseline predictors of response. Results: HbA1c decreased from 7.75 ± 1.01% to 6.80 ± 0.88% after 12 months ($p < 0.00001$). Significant reductions were observed in body weight (−4.09 ± 4.42 kg, $p < 0.00001$), BMI (−1.50 ± 1.55 kg/m^2, $p < 0.00001$) and waist circumference (−5.83 ± 4.71 cm, $p < 0.00001$). Improvements were also detected in lipid profile, blood pressure and visceral adiposity indices. No hypoglycaemic events were reported during follow-up. In multivariable analysis, baseline age, diabetes duration, baseline HbA1c and baseline VAI were not independently associated with the achievement of HbA1c < 7%; therefore, these baseline factors did not discriminate responders within our cohort (hypothesis-generating). Greater absolute HbA1c reductions were observed in patients with higher baseline HbA1c. Conclusions: In older patients with T2DM, oral semaglutide is associated with effective glycaemic control without hypoglycaemia and with a response largely independent of baseline clinical characteristics, supporting its use in elderly and clinically heterogeneous populations.

Keywords: oral semaglutide; older adults; cardiovascular risk; type 2 diabetes; glycaemic control; visceral adiposity indices

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1. Introduction

Type 2 diabetes mellitus (T2DM) represents one of the major public health challenges in the older population, which is characterised by a high burden of comorbidities, clinical frailty, and increased cardiovascular risk [1]. In Italy, data from the AMD Annals confirm a progressively ageing T2DM population followed in diabetes clinics; patients aged >75 years now account for approximately one-third of the cohort (about 36%), and their proportion has increased over recent years [2]. This demographic shift amplifies the need for safe, effective, and simplified treatment strategies tailored to older adults.

In older adults, glucose-lowering treatment is frequently influenced by concerns about adverse events, particularly hypoglycaemia, weight gain, and drug-drug interactions, often leading to therapeutic inertia and suboptimal glycaemic control [3,4]. Accordingly, geriatric diabetes care increasingly emphasises therapeutic de-escalation and regimen simplification, including the replacement or discontinuation of hypoglycaemia-prone therapies such as insulin and sulfonylureas when clinically feasible, to reduce hypoglycaemia risk and treatment burden [4]. This phenomenon is also well documented in Italian clinical practice, where a substantial proportion of older patients fail to achieve recommended glycaemic targets [2].

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) improve glycaemic control through glucose-dependent stimulation of insulin secretion, suppression of inappropriate glucagon secretion, delayed gastric emptying, and reduced appetite, resulting in a low intrinsic risk of hypoglycaemia and favourable effects on body weight and cardiometabolic risk. In cardiovascular outcome trials, several GLP-1 RAs have demonstrated cardiovascular benefit in people with T2DM [5,6]. Current guidelines for older adults emphasise individualised glycaemic targets based on comorbidities, functional status and hypoglycaemia risk, and recommend preferential use of therapies with a low risk of hypoglycaemia when clinically appropriate [4].

Oral semaglutide is the first GLP-1 RA available for oral administration and has shown efficacy in improving glycaemic control and cardiometabolic parameters in randomised clinical trials and real-world settings [7–9]. In geriatric care, an oral formulation may offer practical advantages over injectables, potentially reducing treatment burden and supporting adherence and quality of life in patients who are reluctant or unable to use injections.

Although evidence on oral semaglutide in older adults is expanding, including recent Italian real-world data in elderly cohorts [7,8,10–18], dedicated data remain comparatively limited particularly regarding long-term effectiveness and tolerability across the clinical heterogeneity of older patients (e.g., very old age, multimorbidity and frailty) and the identification of clinically useful predictors of treatment response.

Therefore, the aim of the present study was to evaluate the effectiveness and safety of oral semaglutide in a two-centre real-world population of patients with T2DM aged $\geq$65 years over 12 months, assessing its effects on glycaemic control, major cardiometabolic parameters and visceral adiposity surrogate indices (VAI and LAP), and to explore the association between baseline clinical characteristics and glycaemic response.

2. Materials and Methods

This was a retrospective observational study conducted in patients with type 2 diabetes mellitus aged $\geq$65 years followed in outpatient diabetes clinics at two centres (ASST Garda and ASST Mantova, Italy). Consecutive patients who initiated oral semaglutide between January 2022 and December 2023 were included and followed for 12 months. Oral semaglutide was prescribed according to the approved regimen (3 mg once daily for 30 days, then 7 mg once daily; further dose escalation was at the clinician's discretion). All patients with HbA1c available at baseline (T0) and after 12 months (T1) were included. Missing baseline waist circumference and lipid variables were handled using multiple imputation for the multivariable analyses (see statistical analysis). This manuscript was prepared in accordance with the STROBE statement for observational studies.

A total of 99 consecutive patients initiated oral semaglutide between January 2022 and December 2023. Of these, 81 patients had 12-month HbA1c available and constituted the effectiveness analysis set; early treatment discontinuations are described in the Results section (Adverse Events and Treatment Discontinuations).

2.1. Patient Flow and Analysis Set

2.1.1. Inclusion and Exclusion Criteria

Patients with a diagnosis of type 2 diabetes mellitus, aged ≥65 years, and eligible for treatment with oral semaglutide according to current indications were included. Patients who had modified lipid-lowering or antihypertensive therapy within 90 days before initiation of oral semaglutide, or who required the addition or modification of antidiabetic therapy during follow-up, were excluded. Patients with active malignancy or end-stage chronic kidney disease were also excluded.

2.1.2. Data Collection

Demographic and clinical data were collected for each patient, including age, sex, diabetes duration, body weight, height, body mass index (BMI), waist circumference, and systolic and diastolic blood pressure. Laboratory parameters included glycated haemoglobin (HbA1c), total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, serum creatinine and estimated glomerular filtration rate (eGFR). Data were collected at baseline and at 12-month follow-up.

2.1.3. Metabolic Indices

Indices of visceral adiposity and metabolic risk were calculated using the following formulas (waist circumference, WC, in cm; BMI in kg/m^2). For VAI and LAP calculations, triglycerides (TG) and HDL cholesterol (HDL) were converted to mmol/L.

$$\text{VAI (men)} = [\text{WC}/(39.68 + (1.88 \times \text{BMI}))] \times (\text{TG}/1.03) \times (1.31/\text{HDL})$$

$$\text{VAI (women)} = [\text{WC}/(36.58 + (1.89 \times \text{BMI}))] \times (\text{TG}/0.81) \times (1.52/\text{HDL})$$

$$\text{LAP (men)} = (\text{WC} - 65) \times \text{TG}$$

$$\text{LAP (women)} = (\text{WC} - 58) \times \text{TG}$$

$$\text{TyG index} = \ln [\ \text{TG (mg/dL)} \times \text{fasting plasma glucose (mg/dL)}/2]$$

2.1.4. Study Outcomes

The primary outcome was the achievement of HbA1c < 7% at 12 months. Secondary outcomes included changes from baseline to follow-up in HbA1c, body weight, BMI, waist circumference, lipid profile, blood pressure, renal function and visceral adiposity indices. Associations between baseline clinical characteristics and glycaemic response were also evaluated.

Continuous variables are reported as mean ± standard deviation. Comparisons between baseline and follow-up were performed using paired tests, parametric or non-parametric as appropriate. Associations between changes in clinical and metabolic parameters were explored using Spearman rank correlation (chosen over Pearson because several variables and change scores showed non-normal distributions and potential outliers). Missing baseline waist circumference and lipid variables were handled using Multiple Imputation by Chained Equations (MICEs; 20 imputations). Twenty imputed datasets were generated, including all variables used in the multivariable models and relevant auxiliary variables; regression estimates were pooled according to Rubin's rules. A multivariable logistic regression model was constructed with the achievement of HbA1c < 7% at 12 months as the outcome, including a parsimonious set of clinically relevant baseline covariates (age, diabetes duration, baseline HbA1c, and baseline VAI), in line with events-per-variable considerations. A p value < 0.05 was considered statistically significant.

2.2. Patient Flow (Summary)

- A total of 81 completed 12-month follow-up (effectiveness set).
- A total of 18 discontinued for GI adverse events < 6 months.
- A total of 99 patients initiated oral semaglutide.

Ethical Considerations

The study protocol was approved by the Ethics Committee CET Lombardia 6 (protocol no. 38084/24; promoter: ASST Garda). The study was conducted in accordance with the principles of the Declaration of Helsinki. As a retrospective observational study based on routine clinical data, the analysis was performed on anonymized data.

3. Results

3.1. Study Population and Changes from Baseline

A total of 81 patients aged ≥65 years treated with oral semaglutide were included in the analysis. All subjects had available HbA1c data at baseline (T0) and after 12 months of treatment (T1). The study flowchart is reported in Figure 1.

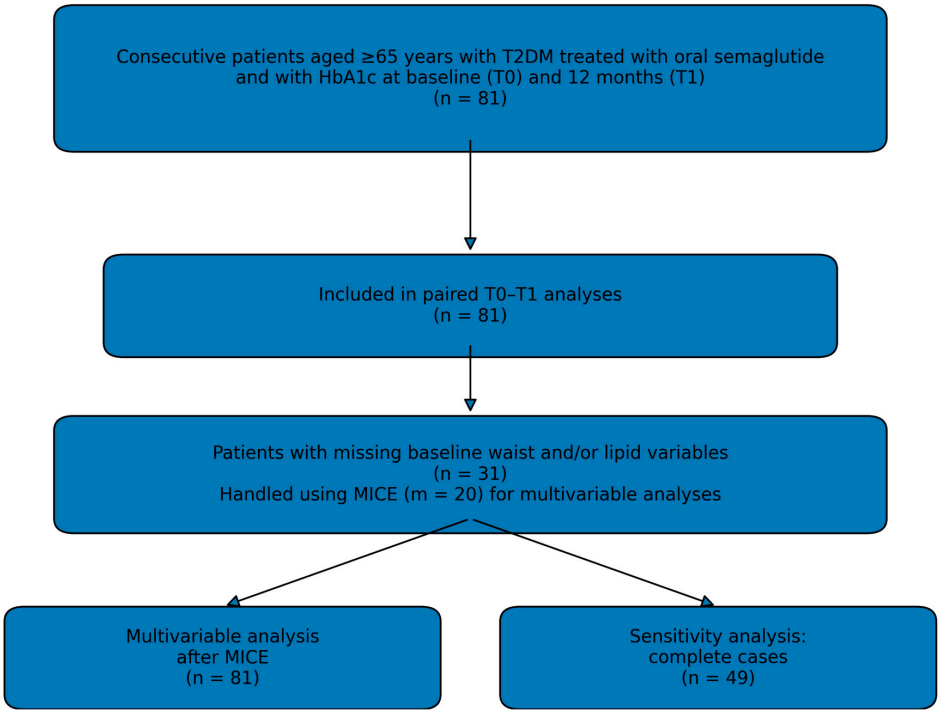


Figure 1. Patient flowchart describing study inclusion, missing baseline data, and analytic samples.

Paired comparisons between T0 and T1 showed significant improvements in glycaemic control, with a mean HbA1c change of −0.96% (95% CI −1.22 to −0.70; n = 81). Body weight decreased by −4.09 kg (95% CI −5.07 to −3.12; n = 81) and BMI by −1.50 kg/m^2 (95% CI −1.85 to −1.16; n = 81). Among patients with available waist measurements (n = 47), waist circumference decreased by −5.83 cm (95% CI −7.21 to −4.45).

Favourable changes were documented in the lipid profile: total cholesterol decreased by −14.73 mg/dL (95% CI −20.80 to −8.66; n = 75), LDL cholesterol by −15.90 mg/dL (95% CI −23.30 to −8.50; n = 73), and HDL cholesterol increased by 3.55 mg/dL (95% CI 2.13 to 4.98; n = 74); triglycerides decreased by −18.07 mg/dL (95% CI −32.05 to −4.08; n = 74). Significant improvements were also observed in visceral metabolic indices, with reductions in the VAI (−0.59; 95% CI −0.87 to −0.32; n = 47), TyG index (−0.15; 95% CI −0.20 to −0.09; n = 74) and LAP index (−19.06; 95% CI −26.92 to −11.19; n = 47).

Renal parameters showed a small but significant decrease in serum creatinine and a corresponding increase in estimated glomerular filtration rate. Systolic and diastolic blood pressure were modestly but significantly reduced over the follow-up period.

Effect sizes were moderate to large for HbA1c, body weight, BMI and waist circumference, supporting the clinical relevance of the observed changes.

The completeness of paired T0-T1 data was ≥90% for most variables, while waist circumference, VAI and LAP index showed lower completeness (58%). To avoid loss of statistical power and potential bias due to complete-case analysis, missing baseline waist circumference and lipid variables were handled using MICEs for the multivariable analyses.

Clinical and metabolic variables are summarized in Table 1.

Table 1. Clinical and metabolic variables at baseline and after 12 months.

Variable	Baseline (T0)	12 Months (T1)	Mean Change (95% CI)	*p* Value
Body weight (kg)	82.96 ± 13.41	78.87 ± 13.40	−4.09 (−5.07 to −3.12)	<0.00001
BMI (kg/m^2)	30.39 ± 4.50	28.88 ± 4.50	−1.50 (−1.85 to −1.16)	<0.00001
Waist circumference (cm)	105.34 ± 8.61	99.51 ± 9.06	−5.83 (−7.21 to −4.45)	<0.00001
HbA1c (%)	7.75 ± 1.01	6.80 ± 0.88	−0.96 (−1.22 to −0.70)	<0.00001
Total cholesterol (mg/dL)	168.49 ± 40.27	153.76 ± 35.43	−14.73 (−20.80 to −8.66)	<0.00001
LDL cholesterol (mg/dL)	89.37 ± 36.91	73.47 ± 31.70	−15.90 (−23.30 to −8.50)	0.00006
HDL cholesterol (mg/dL)	49.99 ± 12.04	53.54 ± 12.00	3.55 (2.13 to 4.98)	<0.00001
Triglycerides (mg/dL)	148.61 ± 66.30	130.54 ± 52.74	−18.07 (−32.05 to −4.08)	0.012
Serum creatinine (mg/dL)	1.05 ± 0.30	1.00 ± 0.29	−0.05 (−0.08 to −0.02)	0.00077
eGFR (mL/min/1.73 m^2)	56.26 ± 17.46	59.65 ± 19.67	3.39 (1.14 to 5.63)	0.0036
Systolic BP (mmHg)	135.56 ± 14.98	131.30 ± 14.68	−4.26 (−7.80 to −0.72)	0.0189
Diastolic BP (mmHg)	77.28 ± 8.26	74.57 ± 7.91	−2.72 (−4.79 to −0.64)	0.011
VAI	2.21 ± 1.36	1.62 ± 0.83	−0.59 (−0.87 to −0.32)	0.00007
TyG index	4.95 ± 0.29	4.80 ± 0.22	−0.15 (−0.20 to −0.09)	<0.00001
LAP index	75.11 ± 38.07	56.05 ± 25.32	−19.06 (−26.92 to −11.19)	0.00001

Values are expressed as mean ± SD. Mean changes are reported with 95% confidence intervals. *p* values refer to paired comparisons between baseline and 12 months. Sample size varies by variable due to missing data.

3.2. Adverse Events and Treatment Discontinuations

Overall, 99 patients initiated oral semaglutide; 18/99 (18.2%) discontinued treatment before 6 months and did not contribute to the 12-month effectiveness analyses. All discontinuations occurred at the 7 mg dose. Discontinuation timing was 6–8 weeks in five patients, 10–12 weeks in five, and >12 weeks in eight. The reasons were gastrointestinal symptoms: nine patients reported mild nausea and dizziness, five reported recurrent vomiting (~three episodes/week), three reported abdominal pain requiring symptomatic medication, and one reported daily diarrhoea with multiple evacuations. No adverse-event-related hospitalizations were recorded. A summary is reported in Table 2.

Table 2. Summary of gastrointestinal adverse events leading to discontinuation (<6 months).

Timing	n	Dose at Stop	Main Symptoms	Hospitalizations
6–8 weeks	5	7 mg	Nausea/dizziness; vomiting	0
10–12 weeks	5	7 mg	Nausea/dizziness; abdominal pain	0
>12 weeks	8	7 mg	Nausea/dizziness; vomiting; diarrhoea	0

When stratified by baseline HbA1c, glycaemic response was clinically graded: mean HbA1c change was −0.46% (95% CI −0.63 to −0.28; n = 22) for baseline HbA1c < 7.0%, −0.54% (95% CI −0.86 to −0.22; n = 33) for HbA1c 7.0–7.9%, and −1.91% (95% CI −2.46 to −1.36; n = 26) for HbA1c ≥ 8.0%. HbA1c reduction was similar across age strata (65–74 years: −0.93%, 95% CI −1.26 to −0.60; n = 51; ≥75 years: −1.01%, 95% CI −1.46 to −0.55; n = 30).

In the multivariable logistic regression model evaluating predictors of achieving HbA1c < 7% at 12 months, performed on the full cohort after multiple imputation (N = 81; MICE, m = 20) and including age, diabetes duration, baseline HbA1c, and baseline VAI, none of these baseline variables were independently associated with the outcome (Table 3). Estimated effects were: age OR 1.02 (95% CI 0.92–1.12), diabetes duration OR 1.00 (95% CI 0.95–1.05), baseline HbA1c OR 0.64 (95% CI 0.39–1.05), and baseline VAI OR 0.99 (95% CI 0.71–1.38). The model showed moderate discriminative ability (mean AUC 0.69 across imputed datasets). We interpret this as suggesting broadly consistent effectiveness across the phenotypes represented in our sample, while acknowledging that modest associations may have gone undetected and that other determinants (e.g., adherence, dose escalation, concomitant therapy changes, and nutritional status/frailty) were not assessed. A sensitivity analysis using complete cases (N = 49) yielded consistent results (AUC 0.71).

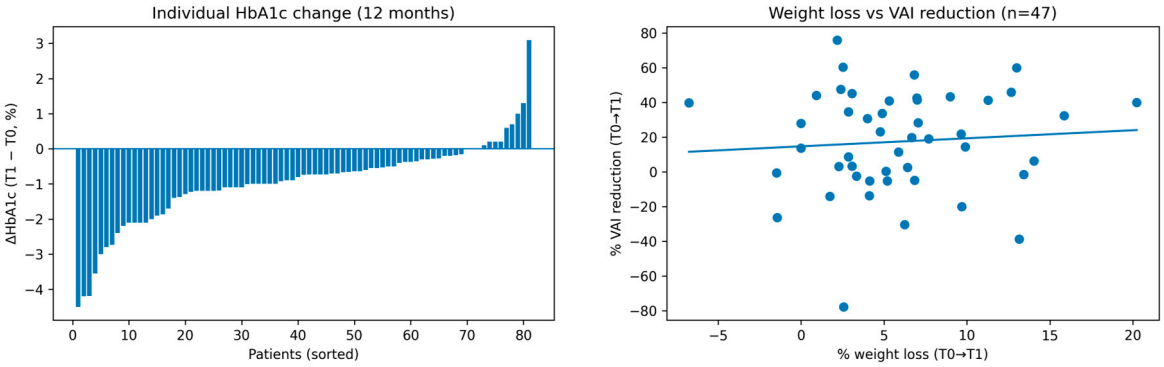
Table 3. Multivariable logistic regression for achievement of HbA1c < 7% at 12 months.

Baseline Variable	OR	95% CI	*p* Value
Age (years)	1.02	0.92–1.12	0.722
Diabetes duration (years)	1.00	0.95–1.05	0.962
Baseline HbA1c (%)	0.64	0.39–1.05	0.077
Baseline VAI	0.99	0.71–1.38	0.958

Multivariable logistic regression model with achievement of HbA1c < 7% at 12 months as the dependent variable. No baseline clinical or metabolic variable was independently associated with the outcome.

Gastrointestinal tolerability was the main reason for early discontinuation during dose escalation; in our cohort, 18.2% of initiators discontinued before 6 months, all at the 7 mg dose, with no hospitalizations. These observations reinforce the need for careful titration and proactive management of GI symptoms in older adults.

Individual changes are shown in Figure 2, and the multivariable model is reported in Table 3.



(**a**) (**b**)

Figure 2. (**a**) Waterfall plot showing individual HbA1c change from baseline (T0) to 12 months (T1) in patients aged ≥65 years, sorted by magnitude of change; (**b**) scatter plot of % weight loss versus % reduction in Visceral Adiposity Index (VAI) from T0 to T1 (n = 47 with available VAI at both timepoints), illustrating the association between weight reduction and improvement in visceral adiposity surrogates.

4. Discussion

In this observational real-world study conducted in patients with type 2 diabetes mellitus aged ≥65 years, treatment with oral semaglutide for 12 months was associated with a clinically and statistically significant improvement in glycaemic control and multiple cardiometabolic parameters, with no hypoglycaemic events reported. The main finding of

the study is the demonstration of a largely homogeneous glycaemic response, independent of major baseline clinical and metabolic characteristics.

In older patients, diabetes management is frequently complicated by multimorbidity, polypharmacy, and frailty, which often lead to a cautious therapeutic approach and, in some cases, undertreatment [3,19–21]. In this context, the risk of hypoglycaemia represents a key determinant in the choice of glucose-lowering therapy [11]. Our findings confirm that oral semaglutide allows significant HbA1c improvement without hypoglycaemic events, reinforcing the favourable safety profile of this agent in older adults.

Although we used the achievement of HbA1c < 7% as a pragmatic endpoint to facilitate interpretability and comparability across studies, we acknowledge that current guidelines recommend individualised glycaemic targets in older adults based on comorbidities, functional status, frailty and hypoglycaemia risk. Therefore, for some patients, less stringent targets may be clinically appropriate; our results should be interpreted within this geriatric framework.

Another relevant finding is the absence of independent baseline predictors of achieving the glycaemic target among the variables tested. Multivariable analysis did not identify age, diabetes duration, body weight, renal function, or visceral adiposity indices as determinants of response in this cohort. We interpret this as supportive of effectiveness that is not confined to a single geriatric clinical phenotype within our sample, rather than as proof that no predictors exist. Other determinants (including adherence, dose escalation and concomitant therapy changes, as well as frailty/nutritional status) may still influence response and warrant investigation in larger comparative studies.

Analysis by baseline HbA1c quartiles showed that patients with higher initial HbA1c values achieved a greater absolute reduction in HbA1c, while reaching comparable final levels. This finding is consistent with previous clinical trials and real-world studies on GLP-1 receptor agonists and reflects a response proportional to the degree of baseline glycaemic dysregulation [9].

Beyond glycaemic control, oral semaglutide treatment was associated with significant reductions in body weight, waist circumference, atherogenic lipid profile, and visceral adiposity indices, resulting in an overall improvement in cardiovascular risk profile. Given the high prevalence of cardiovascular disease in older patients with diabetes, these effects are of particular clinical relevance [5].

From a clinical standpoint, the observed improvements in the lipid profile—including a mean reduction in LDL cholesterol of approximately 16 mg/dL together with lower triglycerides and higher HDL cholesterol—support a shift toward a less atherogenic cardiometabolic profile. Although our study was not designed to evaluate cardiovascular outcomes, these changes are directionally consistent with the broader cardiometabolic benefits reported with GLP-1 receptor agonists in outcome trials and may be particularly relevant in older adults with high baseline cardiovascular risk [5,6].

In geriatric care, intentional weight loss may raise concerns about sarcopenia and functional decline and should be distinguished from involuntary weight loss/cachexia. In older adults with type 2 diabetes, visceral adiposity and dyslipidaemia are major drivers of cardiometabolic risk; therefore, composite indices such as VAI and LAP—integrating waist/BMI with triglycerides and HDL cholesterol—provide pragmatic surrogates of adipose tissue dysfunction beyond body weight alone [10]. Notably, in our cohort weight reduction was accompanied by significant decreases in waist circumference and in surrogate indices of visceral adiposity such as VAI and LAP, which combine anthropometric and lipid measures and are closely linked to visceral fat-related cardiometabolic risk. This pattern supports that the observed weight loss was metabolically favourable, primarily reflecting reduced visceral adiposity rather than catabolic wasting. In line with this, Uchiyama et al.

reported that 24-week oral semaglutide improved glycaemic control with reduction in body fat without significant changes in lean mass or appendicular skeletal muscle index [11,22]. Conversely, a 24-month retrospective cohort study by Ren et al. described reductions in muscle mass and functional measures in older adults treated with semaglutide [12,23], underscoring the importance of individualized risk-benefit assessment and monitoring in frail patients. Recent reviews discuss the potential impact of GLP-1 receptor agonists on body composition and strategies to preserve muscle in older or frail individuals [13,24,25]. Because body composition and muscle function were not directly assessed in our study, sarcopenia-related outcomes cannot be conclusively addressed and should be evaluated in future prospective studies.

Our HbA1c reduction at 12 months (~−0.96%) lies at the higher end of the effect size reported in real-world evidence. Additional contemporary multicentre real-world evidence from the PIONEER REAL programme (e.g., Switzerland and Sweden) and the nationwide Spanish ENDO2S-RWD study also support the effectiveness and tolerability of oral semaglutide in routine care [16–18,26–28]. Recent narrative reviews summarise the rapidly growing real-world evidence base [14,29]. Recent Italian real-world evidence further supports the effectiveness of oral semaglutide in older adults. In the SEMA elderly study by Fiore et al., mean HbA1c decreased from 7.40% to 6.94% at 6 months (−0.44%). In the multicentre Tuscany cohort reported by Baronti et al., HbA1c decreased by −0.87% at both 6 and 12 months overall; in patients aged >75 years, HbA1c reductions were smaller but remained significant (−0.53% at 6 months and −0.54% at 12 months). In our cohort, we observed an HbA1c reduction of −0.96% at 12 months. Differences in baseline glycaemic burden, follow-up duration, and treatment intensification and structured specialist follow-up in routine care may plausibly contribute to these discrepancies; however, cross-study comparisons should be interpreted cautiously [7,8,10–18].

When considering other glucose-lowering strategies, injectable GLP-1 receptor agonists (including subcutaneous semaglutide) have demonstrated robust glycaemic and weight effects; in head-to-head randomised evidence, oral semaglutide provides clinically meaningful HbA1c reductions, while subcutaneous formulations may achieve greater weight loss in some settings [9,15]. In routine geriatric care, the oral formulation may offer practical advantages for patients who are unwilling or unable to use injectable therapies, potentially supporting adherence and treatment persistence. Compared with alternative drug classes that are often preferred in older adults for their low hypoglycaemia risk, GLP-1 receptor agonists additionally target weight and cardiometabolic risk factors, which may be valuable when consistent with the individual patient's goals and tolerance [4].

This study has several limitations. Treatment initiation reflected individualised specialist clinical judgement and shared decision-making; the specific drivers for choosing the oral formulation were multifactorial and not systematically recorded in a structured way in the source records. First, due to the retrospective observational design conducted across a limited number of centres (two) and the absence of a control/comparator group, no causal inference can be made and comparative effectiveness versus other therapies (including injectable GLP-1 receptor agonists or other glucose-lowering drug classes) cannot be established. Second, the relatively small sample size and the 12-month follow-up limit precision and generalizability; therefore, the present findings should be interpreted with caution and considered largely confirmatory of existing real-world evidence rather than hypothesis-changing. Third, subgroup/stratified analyses were exploratory and not powered to detect modest between-strata differences, and standardised measures of frailty and functional status were not available, which prevents aligning outcomes with individualised HbA1c targets. Fourth, incomplete availability of some variables may have limited the power of certain analyses, although multiple imputation was used to mitigate

the missing data impact for the multivariable models. Finally, we did not directly assess body composition or muscle function; therefore, sarcopenia-related outcomes cannot be evaluated. Despite these limitations, the real-world nature of the cohort and the assessment of visceral adiposity surrogates over 12 months provide additional supportive data in an underrepresented geriatric population. Larger multicentre controlled comparative studies are warranted to confirm these results.

5. Conclusions

In this two-centre real-world cohort of adults aged ≥65 years with type 2 diabetes, oral semaglutide was associated with clinically meaningful improvements in HbA1c and multiple cardiometabolic parameters over 12 months, with no hypoglycaemic events observed among patients who completed follow-up.

From a practice perspective, these findings support considering oral semaglutide in older patients when the goals include improving glycaemic control with a low hypoglycaemia risk, reducing visceral adiposity surrogates (VAI/LAP), and simplifying therapy when clinically appropriate (e.g., enabling the reduction in hypoglycaemia-prone agents under specialist supervision). Gastrointestinal tolerability should be actively monitored during titration, and nutritional status and functional reserve should be considered in frail individuals.

In our analyses, none of the pre-specified baseline variables tested independently predicted the achievement of the glycaemic target, suggesting that response in this sample was not restricted to a single geriatric phenotype; this observation should be interpreted cautiously.

These conclusions are limited by the retrospective design, the relatively small sample size, the two-centre setting, and the lack of a comparator group; early discontinuations due to gastrointestinal symptoms occurred and adverse-event severity was not captured using a standardised grading system. Larger prospective comparative studies are needed to confirm these findings and to define robust predictors of response in geriatric populations. Univariable analyses are reported in Table 4.

Table 4. Univariable logistic regression with 95% CI.

Baseline Variable	OR	95% CI	*p*-Value
Age	1.02	0.93–1.11	0.7285
Diabetes duration	1.00	0.95–1.05	0.8901
Baseline HbA1c	0.64	0.40–1.03	0.0634
Baseline VAI	0.85	0.61–1.17	0.3169

Note: Univariable logistic regression (complete case for each predictor); outcome = HbA1c < 7% at 12 months. OR per 1-unit increase; for VAI, N = 49 due to baseline missingness.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki. The patients included in the present analysis were enrolled within a broader institutional protocol approved by the local Ethics Committee; the present work represents a retrospective observational analysis of anonymized data collected during routine clinical practice.

Informed Consent Statement: Patient consent was waived due to the retrospective nature of the study and the use of anonymized data.

Data Availability Statement: The data presented in this study are available on reasonable request from the corresponding author.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

T2DM	Type 2 diabetes mellitus
HbA1c	Glycated haemoglobin
BMI	Body mass index
eGFR	Estimated glomerular filtration rate
GLP-1 RA	Glucagon-like peptide-1 receptor agonist
VAI	Visceral adiposity index
TyG	Triglyceride-glucose index
LAP	Lipid accumulation product
CV	Cardiovascular

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