REGIONE AUTONOMA FRIULI VENEZIA GIULIA

PDTA DEL PAZIENTE CON ICTUS CEREBRALE FASE ACUTA

Prevenzione Secondaria nello Stroke

Stroke a genesi non cardioembolica

- Nel paziente con TIA/Ictus non cardioembolico, a maggior rischio di sanguinamento cerebrale, è indicata terapia con ASA 100-325mg/die nella fase acuta, piuttosto che nessuna terapia (ISOSPREAD), successivamente sostituita da terapia con ASA 100mg/die nella fase cronica, se intolleranza all'ASA è indicata terapia con Clopidogrel (dose di carico 300mg, seguita dadose giornaliera di 75m);
- Nel paziente con TIA/minor Stroke, a basso rischio di sanguinamento, è indicata nella fase acuta terapia con doppia antiaggregazione piastrinica (ASA+Clopidogrel), da valutare in prima giornata l'utilizzo di dose da carico per uno dei due antiaggreganti (ASA 300 o Clopidogrel 300 mg), seguita poi, in seconda giornata, da dosaggio standard ASA100mg+Clopidogrel 75 mg/die (da proseguirsi in maniera continuativa) entro le 24 ore dall'evento fino ai 21 giorni. Solo nei casi selezionati (concomitante patologia cardiaca o severa patologia aterotrombotica) è indicata la prosecuzione di tale terapia fino ai 90 giorni dall'evento ischemico (AHA/ASA 2018, Canadian, ISOSPREAD);
- Nel paziente già in trattamento con antiaggregante piastrinico che sperimenta un nuovo evento ischemico cerebrale è indicato lo shifting verso altro antiaggregante, non è indicato passare ad anticoagulante, non è indicata la triplice antiaggregazione piastrinica (AHA/ASA 2018).

AHA/ASA Guideline

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A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

3.9. Antiplatelet Treatment (Continued)	COR	LOE	New, Revised, or Unchanged
2. In patients presenting with minor noncardioembolic ischemic stroke (NIHSS score ≤3) who did not receive IV alteplase, treatment with dual antiplatelet therapy (aspirin and clopidogrel) started within 24 hours after symptom onset and continued for 21 days is effective in reducing recurrent ischemic stroke for a period of up to 90 days from symptom onset.	I	A	New recommendation.

Results from CHANCE and POINT trials

4. Ticagrelor is not recommended over aspirin for treatment of patients with minor acute stroke.	III: No Benefit	B-R	New recommendation.
The recently completed SOCRATES trial (Acute Stroke or Transient Ischaemic Attack Treated With Aspirin or Ticagrelor and Patient Outcomes) was a randomized, double-blind, placebo-controlled trial of ticagrelor versus aspirin begun within 24 hours in patients with minor stroke (NIHSS score ≤5) or TIA (ABCD2 score ≥4). With a primary outcome of time to the composite end point of stroke, MI, or death up to 90 days, ticagrelor was not found to be superior to aspirin (HR, 0.89 [95% CI, 0.78–1.01]; P=0.07).[219] However, because there were no significant safety differences in the 2 groups, ticagrelor may be a reasonable alternative in stroke patients who have a contraindication to aspirin.			See Table XLVIII in online Data Supplement 1.

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Check for updates

International Journal of Stroke WSO

Canadian stroke best practice recommendations: Secondary prevention of stroke, sixth edition practice guidelines, update 2017

International Journal of Stroke
0(0) 1–24
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Note: These recommendations are applicable to ischemic stroke and transient ischemic attack.

6.1 All patients with ischemic stroke or transient ischemic attack should be prescribed antiplatelet therapy for secondary prevention of recurrent stroke unless there is an indication for anticoagulation [Evidence Level A].

i. Acetylsalicylic acid (80–325 mg daily), combined acetylsalicylic acid (25 mg) and extended-release dipyridamole (25 mg/200 mg twice daily), or clopidogrel (75 mg daily) are all appropriate options and selection should depend on the clinical circumstances [Evidence Level A].
   a. Short-term concurrent use of acetylsalicylic acid and clopidogrel (up to 21 days) has not shown an increased risk of bleeding and may be protective following minor stroke or transient ischemic attack [Evidence Level B].
   b. Longer-term use of acetylsalicylic acid and clopidogrel is not recommended for secondary stroke prevention, unless there is an alternate indication (e.g. coronary drug-eluting stent requiring dual antiplatelet therapy), due to an increased risk of bleeding and mortality [Evidence Level A]. *This combination of efficacy is currently being investigated in the POINT trial (www.Clinicaltrials.gov; Identifier NCT00991029).*

6.2 Pediatric stroke considerations

i. In children with stroke the usual maintenance dosage of acetylsalicylic acid is 3 to 5 mg/kg per day for the prevention of recurrent stroke [Evidence Level B]. The usual maximum dose in adolescents is 81 mg/day.
   a. There is no evidence available on the optimal duration of therapy; this should be based on individual clinical circumstances.
ii. The evidence for clopidogrel use in children is sparse at this time. Clopidogrel may be considered as an alternative for adolescents at a dose of 1 mg/kg/day up to a maximum of 75 mg/day especially in the context of ASA allergy. Younger children may have higher anti-platelet effects of clopidogrel, and the suggested doses should be considered within the range of 0.2–0.5 mg/kg/day [Evidence Level C].

Clinical considerations (New for 2017)

i. At the present time, there is not enough evidence to guide management if a patient has a stroke while on a specific antiplatelet agent. In all cases of recurrent stroke while on antiplatelet therapy, all other vascular risk factors and stroke etiology should be reassessed and aggressively managed.
ii. Expert opinion suggests that if a patient experiences a stroke while on ASA, it may be reasonable to consider switching to clopidogrel; if a patient experiences a stroke while on clopidogrel it may be reasonable to consider switching to combined acetylsalicylic acid (25 mg) and extended-release dipyridamole (200 mg).

Refer to Section 7 on Stroke and Atrial Fibrillation for additional recommendations on anticoagulant therapy.

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Stroke a genesi non cardioembolica

- Nel paziente con TIA/Ictus a genesi aterotrombotica e con stenosi carotidea sintomatica critica (metodo NASCET) è raccomandata la endoarterectomia carotidea (TEA) prima possibile: la TEA è raccomandata nel paziente con stenosi >70% e rischio perioperatorio di morte <6%, la TEA è raccomandata nel paziente con stenosi del 50-69% e rischio perioperatorio di morte <6% in relazione alla morfologia di placca e al rischio di ricorrenza di evento cerebrovascolare (ISOSPREAD, Canadian);
- Nel paziente con TIA/Ictus a genesi aterotrombotica e con stenosi carotidea sintomatica critica la TEA andrebbe eseguita entro i 14 giorni per il paziente non clinicamente stabile, tra le 48h e i 7 giorni nel paziente con stroke minore non disabilitante (mRS 0-2) (AHA/ASA 2018);
- Nel paziente con TIA/Ictus a genesi aterotrombotica e con stenosi carotidea sintomatica critica la scelta di intervento chirurgico vs stenting va ponderata in base al profilo di rischio cardiologico, di recidiva di stroke e di sanguinamento del singolo paziente ed in base all'expertise del singolo centro;

Stroke a genesi non cardioembolica

- Nel paziente con TIA/Ictus e con stenosi carotidea asintomatica la TEA può essere considerata in casi selezionati, lì dove il rischio perioperatorio di morte è <3%: paziente con stenosi ≥70% (in diverse linee guida riportati anche valori >60% fino al 99%, o comunque stenosi >50% con morfologia di placca a rischio) è indicata la TEA se aspettativa di vita >3 anni,

- La migliore terapia medica che include la terapia con statine ad elevato dosaggio e la terapia antiaggregante con ASA+Clopidogrel è indicata in tutti i pazienti con TIA/Ictus e ateromasia carotidea critica fino ad un periodo di 3 mesi;
- Nel paziente con TIA/Ictus e con stenosi intracraniche critiche (70-99% nelle Canadian, 50-99% nelle linee guida AHA/ASA) è indicata la terapia con doppia antiaggregazione piastrinica per un periodo fino ai 90 giorni (Canadian, AHA/ASA), vi sono scarse evidenze circa il beneficio di trattamento con angioplastica intracranica.

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3.13. Emergency Carotid Endarterectomy/Carotid Angioplasty and Stenting Without Intracranial Clot	COR	LOE	New, Revised, or Unchanged
1. The usefulness of emergent or urgent carotid endarterectomy (CEA)/carotid angioplasty and stenting when clinical indicators or brain imaging suggests a small infarct core with large territory at risk (eg, penumbra), compromised by inadequate flow from a critical carotid stenosis or occlusion, or in the case of acute neurological deficit after CEA, in which acute thrombosis of the surgical site is suspected, is not well established.	IIb	B-NR	Recommendation reworded for clarity from 2013 AIS Guidelines. COR unchanged. LOE amended to conform with the ACC/AHA 2015 Recommendation Classification System. See Table XCV in online Data Supplement 1 for original wording.
2. In patients with unstable neurological status (eg, stroke-in-evolution), the efficacy of emergency or urgent CEA /carotid angioplasty and stenting is not well established.	IIb	B-NR	Recommendation reworded for clarity from 2013 AIS Guidelines. COR unchanged. LOE amended to conform with the ACC/AHA 2015 Recommendation Classification System. See Table XCV in online Data Supplement 1 for original wording.

6.7. Carotid Revascularization	COR	LOE	New, Revised, or Unchanged
1. When revascularization is indicated for secondary prevention in patients with minor, nondisabling stroke (mRS score 0–2), it is reasonable to perform the procedure between 48 hours and 7 days of the index event rather than delay treatment if there are no contraindications to early revascularization.	IIa	B-NR	Recommendation revised from 2014 Secondary Prevention.
The risk of recurrent stroke resulting from symptomatic carotid stenosis is highest in the first few days after the initial event.[325–329] Although there is evidence that early or emergency revascularization via either CEA or carotid angioplasty and stenting may be safe in selected cases,[330–332] there are no high-quality prospective data supporting early versus late carotid revascularization in all cases.[333] In cases of minor, nondisabling stroke, a meta-analysis by De Rango et al[326] demonstrates favorable rates of complications when treated at least 48 hours after the initial event, and the risks are not different when treated between 0 to 7 and 0 to 15 days. Revascularization between 48 hours and 7 days after initial stroke is supported by these data in cases of nondisabling stroke (mRS score 0–2).[334]			See Table LXXVIII in online Data Supplement 1.

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Raccomandazione 11.1.e **Debole a favore**

In pazienti con TIA o ictus minore di origine aterotrombotica, giudicati ad alto rischio di recidive (ad esempio per la presenza di microemboli derivanti da placca carotidea alla monitorizzazione con doppler transcranico, o per la presenza di documentata stenosi intracranica), è indicato il trattamento per 1-3 mesi con la doppia antiaggregazione ASA 100 mg + clopidogrel 75 mg.

Raccomandazione 11.1.f **Forte contro** **Grado A**

Il trattamento prolungato - oltre i 90 giorni dall'esordio clinico - con l'associazione di ASA e clopidogrel non è raccomandato per la prevenzione delle recidive di ictus ischemico, perchè comporta un aumento dei rischi emorragici.

Raccomandazione 12.2 **Forte a favore**

L'endoarteriectomia carotidea è raccomandata nella stenosi sintomatica uguale o maggiore del 70% (equivalente a metodo NASCET) se il rischio perioperatorio (fino a 1 mese dall'intervento) di morte e ogni tipo di ictus è inferiore a 6%.

Raccomandazione 12.3 **Forte contro**

L'endoarteriectomia carotidea non è raccomandata nella stenosi sintomatica inferiore al 50% (equivalente a metodo NASCET) oppure in caso di occlusione cronica o di near occlusion della carotide interna.

Raccomandazione 12.4 **Forte a favore**

L'endoarteriectomia carotidea è raccomandata nella stenosi sintomatica compresa fra il 50% ed il 69% (equivalente a metodo NASCET) nel paziente con almeno una delle seguenti condizioni se il rischio perioperatorio (fino a 1 mese dall'intervento) di morte e ogni tipo di ictus è inferiore a 6%:

- ischemia recente (< 2 mesi dal sintomo)
- sintomo cerebrale e non oculare
- placca ulcerata – vulnerabile
- sesso maschile
- assenza di diabete

Raccomandazione 12.5 **Forte a favore**

In caso di stenosi carotidea sintomatica con indicazione a endoarteriectomia è raccomandato eseguire la procedura chirurgica entro le prime due settimane dall'evento ischemico indice.

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Raccomandazione 12.9 **Debole a favore**

L'intervento di endoarteriectomia, in caso di stenosi carotidea asintomatica uguale o maggiore al 70% (equivalente a metodo NASCET), è indicato solo se l'aspettativa di vita del paziente è di almeno 3 anni e se il rischio perioperatorio (fino a 1 mese dall'intervento) di complicanze (morte e ogni tipo di ictus) è inferiore a 3%, con vantaggio dell'intervento tanto maggiore quanto minore è tale rischio.

Raccomandazione 12.10 **Debole a favore**

In caso di stenosi carotidea asintomatica l'endoarteriectomia, comportando un beneficio modesto rispetto alla miglior terapia medica, è indicata nel paziente che è considerato "a rischio" se trattato solo con terapia medica e che presenta quindi almeno una di queste condizioni: pregresso infarto anche silente alla TC/RM encefalo, placca vulnerabile o ulcerata o a rapida crescita, stenosi pre-occlusiva, stenosi tra 70-80% (equivalente a metodo NASCET) con occlusione della carotide controlaterale o con presenza all'ecodoppler transcranico di segnali microembolici omolaterali. E' invece indicata la sola miglior terapia medica nel paziente con aspettativa di vita inferiore a quella presunta per ottenere il beneficio dall'endoarteriectomia, quale il paziente ultraottantenne o con diabete insulino-dipendente o cardiopatia grave o broncopatia grave o insufficienza renale cronica in trattamento dialitico.

Raccomandazione 12.11 **Debole a favore**

In caso di stenosi carotidea asintomatica, ai fini della valutazione del rischio/beneficio della procedura chirurgica, è indicato considerare il punteggio predittivo di rischio periprocedurale di complicanze maggiori (morte, ictus, infarto miocardico). Secondo modelli più recenti, nel paziente con basso punteggio, <4 (corrispondente a rischio periprocedurale <3%), il beneficio atteso dell'endoarteriectomia risulta essere più netto, nel paziente con punteggio intermedio, 4-7 (corrispondente a rischio periprocedurale 3-6%), il beneficio atteso risulta essere marginale, nel paziente con punteggio alto, >7 (corrispondente a rischio periprocedurale >6%), non vi sarebbe alcun beneficio dalla terapia chirurgica per cui sarebbe indicata la sola miglior terapia medica.

Il punteggio viene così assegnato:

- età < 60 anni: 0 punti
- età 60-69 anni: 1 punto
- età 70-79 anni: -1 punto
- età ≥ 80 anni: 2 punti
- dispnea: 2 punti
- broncopatia cronica ostruttiva: 3 punti
- precedente rivascolarizzazione degli arti inferiori o amputazione d'arto: 3 punti
- angina pectoris nel mese precedente: 4 punti
- stato di totale dipendenza per attività quotidiane: 5 punti.

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Stroke a genesi cardioembolica

- Nel paziente con TIA/Ictus a genesi cardioembolica con evidenza di FANV è indicata una terapia con anticoagulanti orali. I DOAC dovrebbero essere preferiti rispetto al Warfarin per il loro migliore profilo di sicurezza (ISOSPREAD, AHA/ASA 2018);
- Nel paziente con TIA/Ictus a genesi cardioembolica e FANV l'utilizzo routinario della bridging therapy con EBPM non è raccomandato (AHA/ASA 2018);
- Nel paziente con TIA/Ictus a genesi cardioembolica che deve iniziare DOAC il timing corretto va dalla 4 alla 14 giornata dall'evento, in base alla severità dell'evento ischemico stesso può essere considerato il seguente schema: entro le 24h per il paziente con TIA, dai 3 ai 5 giorni per lo stroke lieve, dai 6-7 giorni per lo stroke moderato, 12-14 giorni per lo stroke severo;
- In alcuni pazienti con TIA/Ictus e FANV può essere indicata una terapia anticoagulante anche se molto anziani o con decadimento cognitivo, in base al profilo di rischio di sanguinamento di ogni singolo paziente;

Stroke a genesi cardioembolica

- Nel paziente con FANV e pregresso TIA/Ictus a genesi cardioembolica in cui è assolutamente controindicata la terapia con anticoagulanti orali (ad esempio paziente con angiopatia amiloide, in cui è controindicata sia terapia anticoagulante che antiaggregante), in casi selezionati può essere considerata la chiusura dell'auricola sinistra (LAA) per ridurre il rischio di ricorrenza di stroke e tromboembolismo (ESO-CONSENSUS 2018 GRADO C);
- Nel paziente con TIA/Ictus a genesi cardioembolica e FANV in cui è controindicata qualsiasi terapia anticoagulante (DOAC o Warfarin), è raccomandata la terapia con ASA 100mg/die (Canadian);
- Nel paziente con TIA/Ictus a genesi cardioembolica con evidenza di FANV è indicata una terapia con anticoagulanti orali, l'associazione di eventuale terapia antiaggregante va valutata da caso a caso a seconda del rischio di ricorrenza di patologia cerebro e cardiovascolare (paziente con angina instabile/stenting coronarico) e sulla base del profilo di rischio di sanguinamento del singolo paziente (AHA/ASA 2018).

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6.6.2. Atrial Fibrillation	COR	LOE	New, Revised, or Unchanged
1. For most patients with an AIS in the setting of atrial fibrillation, it is reasonable to initiate oral anticoagulation between 4 and 14 days after the onset of neurological symptoms.	**IIa**	**B-NR**	Recommendation revised from 2014 Secondary Prevention.
A multicenter prospective cohort of 1029 patients with AIS and newly diagnosed atrial fibrillation showed a better composite outcome of stroke, TIA, systemic embolism, sICH, and major extracranial bleeding within 90 days when anticoagulant was initiated 4 to 14 days from stroke onset (HR 0.53 [95% CI, 0.30–0.93] for starting anticoagulation at 4–14 days compared with <4 days); high CHA_2DS_2-VASc score, high NIHSS score, large ischemic lesions, and type of anticoagulation were associated with poorer outcomes.[378] In a prospective, open-label study of 60 patients with atrial fibrillation and either mild to moderate AIS with NIHSS score <9 (n=49) or TIA (n=11) who were treated with rivaroxaban within14 days of onset, 50 were available for follow-up at 7 days after drug initiation. None developed symptomatic hemorrhagic transformation (HT). Of the 23 with AIS who had HT at baseline, 5 demonstrated asymptomatic radiographic progression, and 18 showed neither clinical nor radiographic progression. Of the remaining 27 who did not have HT at baseline, 3 developed asymptomatic HT.[227]			See Table LI in online Data Supplement 1.
2. For patients with a history of ischemic stroke, atrial fibrillation, and coronary artery disease, the usefulness of adding antiplatelet therapy to oral anticoagulants is uncertain for purposes of reducing the risk of ischemic cardiovascular and cerebrovascular events. Unstable angina and coronary artery stenting represent special circumstances in which management may warrant dual antiplatelet/oral anticoagulation.	**IIb**	**C-LD**	Recommendation reworded for clarity from 2014 Secondary Prevention. COR unchanged. LOE amended to conform with ACC/AHA 2015 Recommendation Classification System. See Table XCV in online Data Supplement 1 for original wording.

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Stroke a genesi cardioembolica

- Nel paziente con Ictus emorragico e FANV in cui è indicata la terapia anticoagulante, la stessa va ripresa dopo l'emorragia per i pazienti a elevato rischio di embolismo cerebrale/sistemico. I DOAC sono da preferire al Warfarin;
- Il timing per l'introduzione della terapia anticoagulante non è ancora sempre ben definito. Per i DOAC può essere considerato ragionevole iniziare tra la 7° e 8° settimana dopo l'evento (studi osservazionali), per gli antagonisti della vitamina K tra la 10° e 30° settimana;

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6.6.4. Hemorrhagic Transformation	COR	LOE	New, Revised, or Unchanged
1. For patients with AIS and HT, initiation or continuation of antiplatelet or anticoagulation therapy may be considered, depending on the specific clinical scenario and underlying indication.	**IIb**	**C-LD**	Recommendation revised from 2014 Secondary Prevention.
Several observational studies suggest that antithrombotics can be safely initiated or continued in patients with AIS and HT. In a prospective, open-label study of 60 patients with atrial fibrillation and either mild to moderate AIS with an NIHSS score <9 (n=49) or TIA (n=11) who were treated with rivaroxaban within 14 days of onset, 50 were available for follow-up at 7 days after drug initiation. None developed symptomatic HT. Of the 23 with AIS who had HT at baseline, 5 demonstrated asymptomatic radiographic progression, and 18 showed neither clinical nor radiographic progression. Of the remaining 27 who did not have HT at baseline, 3 developed asymptomatic HT.[227] A retrospective stroke registry analysis identified 222 patients with AIS and HT. The frequency of composite events (neurological deterioration, vascular events, and death) at 1 month was significantly lower in patients treated with antithrombotics compared with those who were not (1.6% versus 11.1%; *P*=0.041). Neither antiplatelet (n=72) nor anticoagulant (n=28) treatment after HT was associated with enlargement of the original HT or development of new HT or neurological deterioration.[382] Individual assessment of the clinical indication, benefits, and associated risks is warranted.[10,382,383]			See Table LI in online Data Supplement 1.

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Stroke a genesi cardioembolica

- Nel paziente con TIA/Ictus e diagnosi di PFO senza evidenza di altra patologia emboligena (TVP/EP) e indicazione a terapia anticoagulante o a chiusura del PFO è indicata una terapia antiaggregante (ISOSPREAD);
- Nel paziente con TIA/Ictus e diagnosi di PFO, dopo discussione multidisciplinare del caso e valutazione del profilo di rischio di embolismo cerebrale del paziente (Rope Score) è indicata la chiusura del PFO e la terapia antiaggregante in maniera continuativa, secondo le seguenti indicazioni: paziente tra i 18 e i 60 anni con TIA/Ictus criptogenico e PFO ad elevato rischio (caratteristiche morfologiche del PFO) è raccomandata la chiusura percutanea del PFO e la terapia medica (antiaggregante) vs solo terapia medica (ESO-CONSENSUS 2018 GRADO A); paziente tra i 60-65 anni con TIA/Ictus criptogenico e PFO ad elevato rischio (caratteristiche morfologiche del PFO) può essere offerta la chiusura percutanea del PFO e la terapia medica (antiaggregante) vs solo terapia medica (ESO-CONSENSUS 2018 GRADO B); paziente con età <18 anni o >65 anni con TIA/Ictus criptogenico e PFO ad elevato rischio (caratteristiche morfologiche del PFO) può essere indicata la chiusura percutanea del PFO e la terapia medica (antiaggregante) vs solo terapia medica su base individuale (ESO-CONSENSUS 2018 GRADO C);
- Non vi sono ancora evidenze circa la superiorità della chiusura del PFO vs terapia anticoagulante.

EUROPEAN STROKE JOURNAL

Consensus statements and recommendations from the ESO-Karolinska Stroke Update Conference, Stockholm 11–13 November 2018

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Q1: Does percutaneous closure of PFO versus antiplatelet therapy reduce the risk of stroke recurrence?

Recommendation: In patients aged 18–60 years old with cryptogenic stroke/TIA and with high risk PFO features (moderate or severe shunt, atrial septal aneurysm (ASA), atrial septal hypermobility) we recommend percutaneous closure plus medical therapy instead of antiplatelet therapy alone (Grade A).

In patients between 60 and 65 years, percutaneous closure plus medical therapy instead of antiplatelet therapy alone can be offered (Grade B).

Percutaneous closure plus medical therapy can be considered in place of antiplatelet therapy alone also for patients aged <18 and >65 years old on an individual basis (Grade C).

Q2: Does percutaneous closure of PFO versus oral anticoagulants reduce the risk of stroke recurrence?

Recommendation: Based on the few available data, percutaneous closure and Oral anticoagulation (OAC) therapy seem to perform equally (Grade C). Therefore, while waiting for further evidence and based on the superiority of percutaneous closure over medical therapy as a whole, patient engagement in the choice becomes pivotal.

Adequately dimensioned randomised clinical trials addressing the comparison between percutaneous closure plus medical therapy versus OAC (vitamin-K antagonists or direct OAC) in carefully characterised patients with cryptogenic cerebrovascular accident and different risk characteristics, should be performed.

Q3: Does oral anticoagulant therapy versus antiplatelet therapy reduce the risk of stroke recurrence?

Recommendation: In patients in whom a medical therapy only is chosen, we recommend to choose the specific drugs weighing the individual risk of bleeding against the risk of PFO-related stroke recurrence, in close connection with the patient. Long-term OAC with vitamin K antagonists (VKAs) may be preferred if: (a) the patient has a low haemorrhagic risk, (b) a probable good therapeutic compliance is foreseen and (c) a proper anticoagulant monitoring can be guaranteed (Grade B).

We recommend to perform adequately dimensioned head-to-head randomised clinical trials addressing the comparison between single antiplatelet drugs versus OAC (vitamin-K antagonists or Direct oral anticoagulants (DOAC)) in patients in which percutaneous closure has been excluded.

Stroke a genesi non cardioembolica: dissezione carotidea/vertebrale extracranica ed intracranica

- Nel paziente con TIA/Ictus non cardioembolico e dissezione carotidea o vertebrale extracranica è indicata terapia antiaggregante o anticoagulante per un periodo dai 3 ai 6 mesi, ci sono poche evidenze circa l'ottimale durata di terapia (AHA/ASA 2018);
- Nel paziente con TIA/Ictus non cardioembolico e dissezione carotidea o vertebrale extracranica che presenta eventi ischemici ricorrenti, nonstante la terapia medica in atto, il beneficio di stenting extracranico non è ben definito (AHA/ASA 2018);
- Nel paziente con dissezione intracranica vi sono scarse evidenze circa il beneficio del trattamento con anticoagulanti.

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6.6.3. Arterial Dissection	COR	LOE	New, Revised, or Unchanged
1. For patients with AIS and extracranial carotid or vertebral arterial dissection, treatment with either antiplatelet or anticoagulant therapy for 3 to 6 months is reasonable.	IIa	B-NR	Recommendation revised from 2014 Secondary Prevention.
Although there has not been a randomized trial of antithrombotic therapy versus placebo in patients with acute cervical artery dissection (CeAD), numerous observational studies and expert opinion suggest that it is reasonable to initiate antithrombotic therapy in the acute setting to prevent early thromboembolic events. The CADISS (Cervical Artery Dissection in Stroke Study) group published a randomized, open-label phase II feasibility trial of anticoagulation versus antiplatelet therapy in 250 participants with extracranial carotid or vertebral artery dissection recruited from 46 centers in the United Kingdom and Australia.[379] The primary outcome was ipsilateral stroke or all-cause mortality within 3 months of randomization in an intention-to-treat analysis, and there were no significant differences between groups. There was also no difference in rates of major bleeding. As a phase II trial, the study concluded that a definitive phase III trial would not be feasible, primarily because of the low event rates in both groups. Additional limitations included a lack of central radiological confirmation in 20% of cases and a mean time to randomization of 3.65 days that perhaps limits generalizability of the results to the hyperacute period. Nonetheless, the CADISS trial supports numerous previous observational studies that found no significant difference in clinical outcomes with the use of anticoagulation compared with antiplatelet therapy in patients with CeAD. In addition, in a follow-up CADISS analysis of dissecting aneurysms (DAs), there was no association between treatment allocation (antiplatelets versus anticoagulants) and whether DAs at baseline persisted at follow-up or whether new DAs developed. During 12 months of follow-up, stroke occurred in 1 of 48 patients with DA and in 7 of 216 patients without DA (age- and sex-adjusted OR, 0.84 [95% CI, 0.10–7.31]; *P*=0.88). A review of published studies, mainly retrospective, showed a similarly low risk of stroke and no evidence of an increased stroke rate in patients with DA.[380] These data provide evidence that DAs may have a benign prognosis, and therefore, medical treatment should be considered.			See Tables LI and XC in online Data Supplement 1.
2. For patients with AIS and extracranial carotid or extracranial vertebral arterial dissection who have definite recurrent cerebral ischemic events despite medical therapy, the value of extracranial EVT (stenting) is not well established.	IIb	C-LD	Recommendation revised from 2014 Secondary Prevention.
There have been no controlled trials of EVT and stenting in patients with extracranial CeAD. The published literature reflects small case series, individual case reports, and several systematic reviews.[381] A systematic review of the literature published until 2009 found 31 published reports (N=140) with a technical success rate of 99% and procedural complication rate of 1.3%. However, these observational data are prone to selection and reporting biases. A retrospective analysis of patients with CeAD (n=161) comparing extracranial EVT (with and without stenting) with medical therapy alone found no difference in 90-day outcomes (adjusted OR, 0.62 [95% CI, 0.12–3.14]; *P*=0.56). With medical therapy alone, the overall prognosis and natural history of CeAD, including DAs, are favorable.[379,380] Therefore, the benefit of extracranial EVT and stenting in patients with CeAD and definite recurrent cerebral ischemic events despite medical therapy is not well established.			See Table LI in online Data Supplement 1.

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International Journal of Stroke WSO

Canadian stroke best practice recommendations: Secondary prevention of stroke, sixth edition practice guidelines, update 2017

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8.4 Cervicocephalic artery dissection (new for 2017)

i. A diagnosis of carotid or vertebral dissection can be established by CTA, MRA, or DSA [Evidence Level C].

Note: CTA or MRA are the preferred noninvasive diagnostic imaging tests for patients with a suspected cervicocephalic artery dissection, as neck ultrasound does not fully visualize the vertebral arteries and can miss distal or carotid dissection originating above the angle of the jaw.

ii. Antithrombotic therapy for stroke prevention is recommended for individuals with a diagnosis of an extracranial carotid or vertebral artery dissection [Evidence Level B].
   a. There is uncertainty about the comparative efficacy of antiplatelet therapy vs. anticoagulation with heparin/warfarin; either treatment is considered reasonable and decision should be based on individual risk/benefit analysis [Evidence Level B].
   b. There is a lack of evidence regarding the optimal duration of antithrombotic therapy and the role of repeat vascular imaging in decision-making. Decisions may be based on individual clinical factors [Evidence Level C].

Note: There is insufficient evidence at this time to make a recommendation regarding the use of DOACs in patients with arterial dissections.

iii. There is a lack of evidence regarding the use of anticoagulation in intracranial arterial dissection. Decisions may be based on individual clinical factors [Evidence Level C].

Gestione dei fattori di rischio

- Nel paziente con TIA/Ictus è raccomandato il controllo dei valori pressori per raggiungere un target di 140/90 mmHg, nel paziente con diabete mellito il target da raggiungere è di 130/80 mmHg, quest'ultimo target è quello consigliato anche nel paziente con epatopatia,
- Nel paziente con TIA/Ictus per il controllo dei valori pressori i farmaci da preferire sono nell'ordine gli ACE-Inibitori, Calcioantagonisti e Diuretici;
- Nel paziente con TIA/Ictus è raccomandato il controllo lipidico ponendo attenzione ai valori di LDL con l'obiettivo di ridurre i valori di LDL >50% rispetto ai valori al baseline o di mantenere i valori di LDL <70 mg/dL;
- Nel paziente con TIA/Ictus è raccomandato l'utilizzo di Statine per il migliore controllo lipidico, i maggiori benefici sono stati riscontrati con l'impiego di Atorvastatina 80mg/die, gli inibitori di PCSK9 possono rappresentare un'alternativa terapeutica all'associazione Statina+Ezetimibe nel controllare i livelli di LDL;
- Nel paziente con TIA/Ictus è raccomandato l'utilizzo di Statine soprattutto se sono presenti altri fattori di rischio tra cui il diabete mellito;
- Nel paziente con TIA/Ictus è raccomandato il controllo dei valori glicemici mantenendo come obiettivo di compenso glicemico l'emoglobina glicata ≤7-8% (sia per DM tipo I che per DM tipo II), il controllo glicemico va ottimizzato per singolo paziente: nei soggetti anziani con pluricomorbidità e con storia di DM>10 anni è ragionevole ottenere un compenso glicemico con emoglobina glicata ≤8%, nel paziente più giovane con storia più recente di DM i valori attesi sono ≤7%, un controllo glicemico più stretto (valori di emoglobina glicata ≤6,5%) può essere preso in considerazione per il paziente con recente storia di malattia (DM), assenza di patologia cardiovascolare e lunga aspettativa di vita;

Gestione dei fattori di rischio

- Nel paziente con TIA/Ictus è raccomandato un introito giornaliero di sodio che non superi i 2000mg/die;
- I pazienti con TIA/Ictus dovrebbero essere incoraggiati a svolgere regolare attività fisica;
- I pazienti con TIA/Ictus dovrebbero essere incoraggiati a mantenere un BMI tra i 18,5 e i 24,9 Kg/m2, o avere una circonfrenza addominale <88 cm per la donna e <102 cm per l'uomo;
- I pazienti con TIA/Ictus dovrebbero limitare l'introito alcolico a 10 drinks/settimana (non più di due drinks/die) per la donna e 15 drinks/settimana (non più di tre drinks/die) per l'uomo;
- Nel pazienti con TIA/Ictus è fortemente scoraggiato l'uso di droghe o altre sostanze di abuso;
- I pazienti con TIA/Ictus vanno istruiti sulla necessità di astensione dal fumo, può essere presa in considerazione la somministrazione di Nicotine replacement durante l'ospedalizzazione o nella fase acuta dell'astensione;
- Nel paziente con TIA/Ictus dovrebbe essere scoraggiata l'assunzione di estroprogestinici;
- Nel paziente con TIA/Ictus è raccomandato il trattamento dei disturbi del sonno come le OSAS.

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

6.9. Institution of Antihypertensive Medications	COR	LOE	New, Revised, or Unchanged
1. Starting or restarting antihypertensive therapy during hospitalization in patients with BP >140/90 mm Hg who are neurologically stable is safe and is reasonable to improve long-term BP control unless contraindicated.	**IIa**	**B-R**	New recommendation.
Starting or restarting antihypertensive medications has been shown to be associated with improved control of the BP after discharge in 2 trials.[247,248] Therefore, it is reasonable to start or restart antihypertensive medications in the hospital when the patient remains hypertensive and is neurologically stable. Studies evaluating this question included only patients with previous diagnosis of hypertension[247] or enrolled mostly patients with previous hypertension.[248] However, because hypertension is not uncommonly first diagnosed during the hospitalization for stroke, it is reasonable to apply this recommendation also to patients without preexistent hypertension.			See Table LVI in online Data Supplement 1.

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A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

6.8.1. General Principles	COR	LOE	New, Revised, or Unchanged
1. Patients with AIS should be managed according to the 2018 ACC/AHA Cholesterol Guidelines, which include lifestyle modification, dietary recommendations, and medication recommendations.	I	A	Recommendation, COR, and LOE updated from 2014 Secondary Prevention to reference 2018 Cholesterol Guidelines
The 2018 Cholesterol Guidelines provide a comprehensive set of recommendations for managing hyperlipidemia.[19] Those recommendations that are most pertinent to the in-hospital management of patients with AIS are excerpted here. The full guidelines should be used for guidance in managing these disorders in patients with AIS and for supporting evidence.			
2. In adults who are 20 years of age or older and not on lipid-lowering therapy, measurement of either a fasting or a nonfasting plasma lipid profile is effective in estimating atherosclerotic cardiovascular disease (ASCVD) risk and documenting baseline low-density lipoprotein cholesterol (LDL-C).	I	B-NR	Recommendation unchanged from 2018 Cholesterol Guidelines.
3. Adherence to changes in lifestyle and effects of LDL-C–lowering medication should be assessed by measurement of fasting lipids and appropriate safety indicators 4 to 12 weeks after statin initiation or dose adjustment and every 3 to 12 months thereafter based on need to assess adherence or safety.	I	A	Recommendation unchanged from 2018 Cholesterol Guidelines.

6.8.2. Choice of Lipid-lowering Drugs for Patients with Clinical ASCVD*	COR	LOE	New, Revised, or Unchanged
1. In patients who are 75 years of age or younger with clinical ASCVD, high-intensity statin therapy should be initiated or continued with the aim of achieving a 50% or greater reduction in LDL-C levels.	I	A	Recommendation unchanged from 2018 Cholesterol Guidelines.
2. In patients with clinical ASCVD in whom high-intensity statin therapy is contraindicated or who experience statin-associated side effects, moderate-intensity statin therapy should be initiated or continued with the aim of achieving a 30% to 49% reduction in LDL-C levels.	I	A	Recommendation unchanged from 2018 Cholesterol Guidelines.

Lipid management: ISO and Canadian

Raccomandazione 11.4 **Forte a favore** **Grado A**

Nei casi di ictus e TIA di natura non cardioembolica, non necessariamente con colesterolo elevato ma con livello di LDL superiore a 100 mg/dL, è raccomandato l'utilizzo di statine perché determinano una riduzione degli eventi ischemici maggiori.

4.2 Lipid management

i. Patients with ischemic stroke or transient ischemic attack should be managed with aggressive therapeutic lifestyle changes to lower lipid levels, including dietary modification, as part of a comprehensive approach to lower risk of first or recurrent stroke unless contra-indicated [Evidence Level B]. *Refer to Prevention of Stroke Module, Section 2 for Lifestyle Management recommendations.*

ii. A statin should be prescribed for secondary prevention in patients who have had an ischemic stroke or transient ischemic attack in order to achieve a target LDL cholesterol consistently less than 2.0 mmol/L or >50% reduction of LDL cholesterol, from baseline [Evidence Level B].[36]

   a. For individuals with stroke and acute coronary syndrome or established coronary disease, treatment to more aggressive targets (LDL-C <1.8 mmol/L or >50% reduction) should be considered [Evidence Level A].

iii. Adults with diabetes and ischemic stroke are at high risk of further vascular events and should also be treated with a statin to achieve a LDL cholesterol ≤2.0 mmol/L [Evidence Level B].

iv. Statin therapy is not indicated for prevention of intracerebral hemorrhage [Evidence Level B].

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6.4. Glucose	COR	LOE	New, Revised, or Unchanged
1. After AIS, it is reasonable to screen all patients for diabetes mellitus with testing of fasting plasma glucose, hemoglobin A_{1c}, or an oral glucose tolerance test. Choice of test and timing should be guided by clinical judgment and recognition that acute illness may temporarily perturb measures of plasma glucose. In general, hemoglobin A_{1c} may be more accurate than other screening tests in the immediate postevent period.	IIa	C-EO	Recommendation wording modified from 2014 Secondary Prevention to match COR IIa stratifications and reworded for clarity. COR unchanged. LOE amended to conform with ACC/AHA 2015 Recommendation Classification System. See Table XCV in online Data Supplement 1 for original wording.

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Diabetes management: Canadian

5.2 Diabetes management

i. Glycemic targets should be individualized; however, lowering A1C values to ≤7% in both type 1 and type 2 diabetes and stroke or transient ischemic attack, provides strong benefits for the prevention of microvascular complications [Evidence Level A].

ii. To achieve a target of A1C ≤7.0%, most patients with type 1 or type 2 diabetes should aim for a fasting plasma glucose or preprandial plasma glucose target of 4.0 to 7.0 mmol/L [Evidence Level B].

iii. The 2-hour postprandial plasma glucose target is 5.0 to 10.0 mmol/L [Evidence Level B]. If A1C targets cannot be achieved with a postprandial target of 5.0 to 10.0 mmol/L, further postprandial blood glucose lowering, to 5.0 to 8.0 mmol/L, should be considered [Evidence Level C].

Note: For recommendations on the use of SGLT2 inhibitors, please refer to the current Diabetes Canada guidelines at www.diabetes.ca.

Clinical considerations (New for 2017)

i. The results from a recent trial, *Pioglitazone after Ischemic Stroke or Transient Ischemic Attack*[41] suggested that while there is a benefit of pioglitazone for stroke prevention in patients with positive insulin resistance, it is offset by the increased risk of fractures and bladder cancer. The decision to use this agent could be considered based on the specific risk profile for each patient.

ii. More intensive glucose control (A1C ≤6.5%), may be considered in patients with a shorter duration of diabetes, no evidence of significant cardiovascular disease and longer life expectancy, provided this does not result in a significant increase in hypoglycemia (Diabetes Canada 2016).

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Diabetes management: ISO and ASA/AHA

Raccomandazione 7.10.a **Debole a favore**

La diagnosi e la terapia del diabete mellito, unitamente al miglior controllo della glicemia a digiuno e post-prandiale, sono indicati per la riduzione del rischio di ictus.

Raccomandazione 7.10.b **Forte a favore**

Obiettivi di compenso glicemico meno stringenti (HbA1c ≤64 mmol/mol [≤8,0%]) sono raccomandati in pazienti con diabete di lunga durata (>10 anni) soprattutto con precedenti di malattie cardiovascolari o una lunga storia di inadeguato compenso glicemico o fragili per età e/o comorbilità. L'approccio terapeutico deve essere mirato alla prevenzione delle ipoglicemie.

Glucose disorders

After a TIA or ischemic stroke, all patients should probably be screened for DM with testing of fasting plasma glucose, HbA_{1c}, or an oral glucose tolerance test. Choice of test and timing should be guided by clinical judgment and recognition that acute illness may temporarily perturb measures of plasma glucose. In general, HbA_{1c} may be more accurate than other screening tests in the immediate postevent period *(Class IIa; Level of Evidence C)*.

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Sleep Apnea: ASA/AHA

Sleep Apnea Recommendations

1. **A sleep study might be considered for patients with an ischemic stroke or TIA on the basis of the very high prevalence of sleep apnea in this population and the strength of the evidence that the treatment of sleep apnea improves outcomes in the general population *(Class IIb; Level of Evidence B)*.** (New recommendation)
2. **Treatment with CPAP might be considered for patients with ischemic stroke or TIA and sleep apnea given the emerging evidence in support of improved outcomes *(Class IIb; Level of Evidence B)*.** (New recommendation)

2. Routine screening of patients with recent ischemic stroke for obstructive sleep apnea (OSA) is not recommended.	**III: No Benefit**	**B-R**	New recommendation.
Numerous studies have established an association between OSA and stroke. OSA is highly prevalent among ischemic stroke patients and has been associated with considerable morbidity, including increased risk of cardiovascular and cerebrovascular events, worse prognosis, and higher mortality. Continuous positive airway pressure (CPAP) remains the most effective medical therapy for OSA.[366–370] A small RCT of CPAP in 127 patients started 4.6±2.8 days after AIS showed mixed results with no effect on disability, total cardiovascular events, cardiovascular mortality, or cardiovascular event–free survival but a reduction in time to first cardiovascular event during 24-month follow-up. This trial did not specify a primary end point and compared multiple different outcomes at multiple time points.[371] The SAVE RCT (Continuous Positive Airway Pressure Treatment of Obstructive Sleep Apnea to Prevent Cardiovascular Disease) randomized 2717 patients with established cardiovascular or cerebrovascular disease (but not within the first 90 days after a stroke except for minor strokes) and moderate to severe OSA to CPAP versus usual care without CPAP and found no reduction of vascular events, including stroke, in patients treated with CPAP over a mean follow-up of 3.7 years.[372] Thus, the routine screening for OSA of all patients with AIS for the secondary prevention of cardiovascular events or death is not recommended at this time. Several ongoing National Institutes of Health–funded RCTs are further investigating the effects of CPAP in patients with AIS and OSA (NR018335, NS099043).			See Table LXXXVI in online Data Supplement 1.

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