Association of Hong Kong Diabetes Nurses
Evidence-based Practice Committee
Insulin Injection Forum

How should lipohypertrophy and lipoatrophy be managed?

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Lipodystrophy

1. **Injection into the hypertrophic and atrophic areas should be avoided**. 1,21,49,53 (II A)

2. Training to Health Care Professionals is required to identify lipohypertrophic lesions. 31,32 (IIA)

3. Visual inspection and palpation of injection area by the health care professionals should be performed routinely and documented. 36,39,50,83 (III B)

4. Intensive patient training on injection technique, **systematic rotation** and frequent inspection is effective to improve and prevent lipohypertrophy. 17,73 (IA)

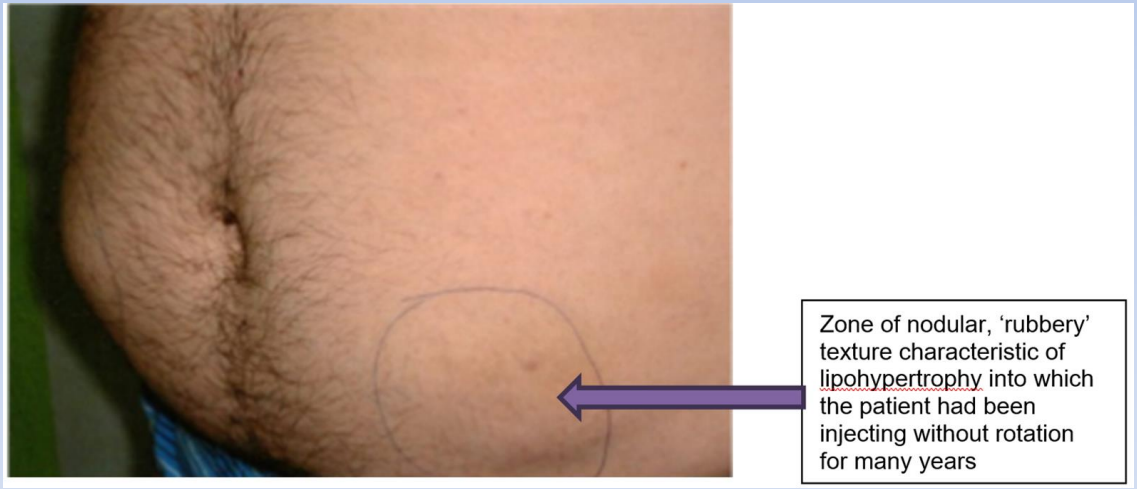
5. A decrease of **insulin dose** may be required when switching injection from areas of lipohypertrophy to normal tissue and should be guided by blood glucose measurement. 21 (II B)

Content

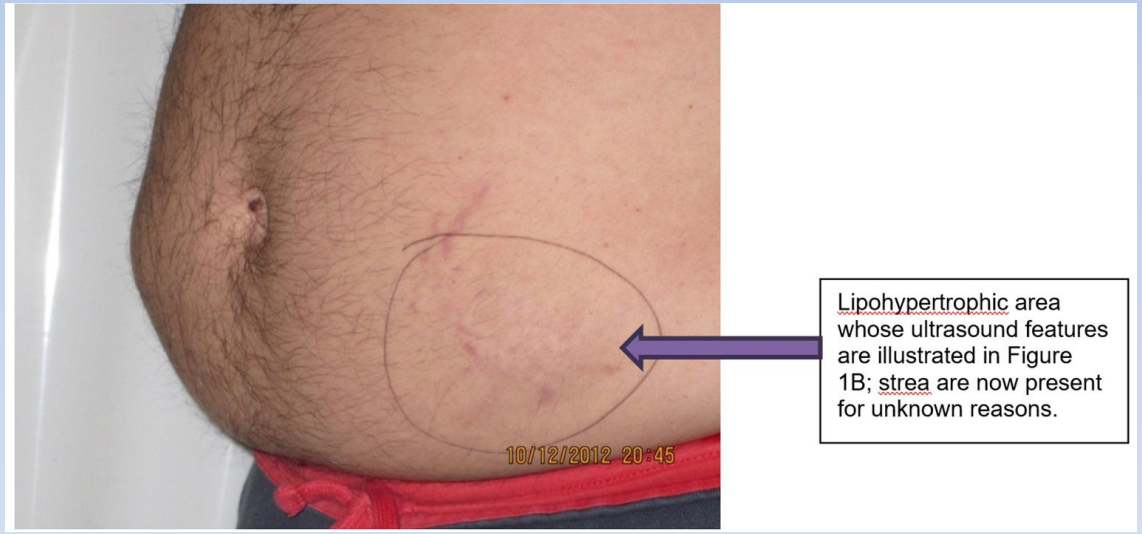
- Clinical features
- Consequences
- Prevalence
- Risk factors
- **Assessment** of lipohypertrophy
  - Checklist for lipohypertrophy assessment
  - Palpation technique and maneuvers
  - Video
- **Documentation**
- Proposed method to prevent lipohypertrophy
- Take home message

Clinical Lipohypertrophy

August 2012



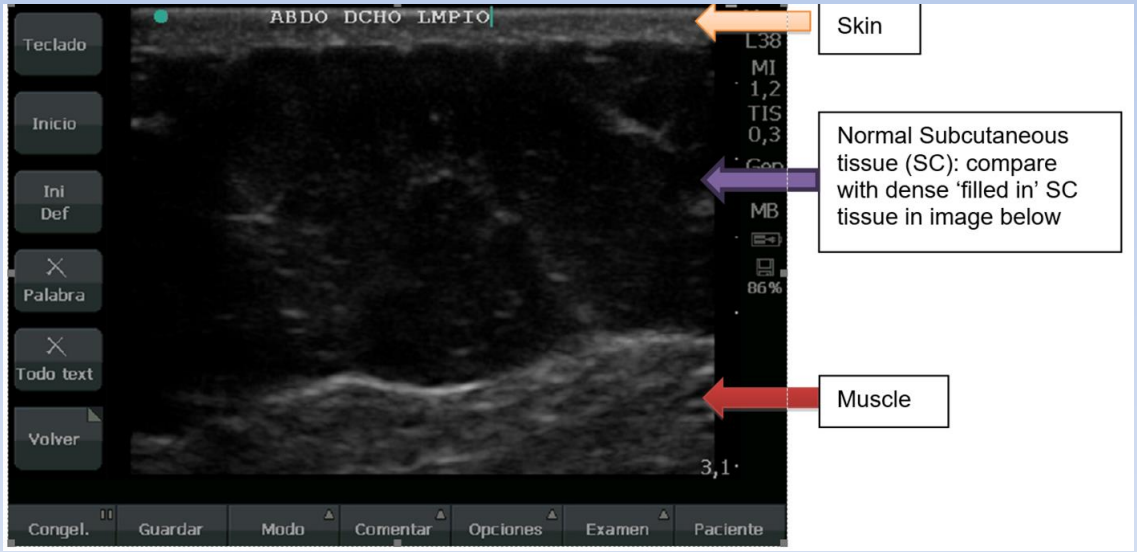
December 2012



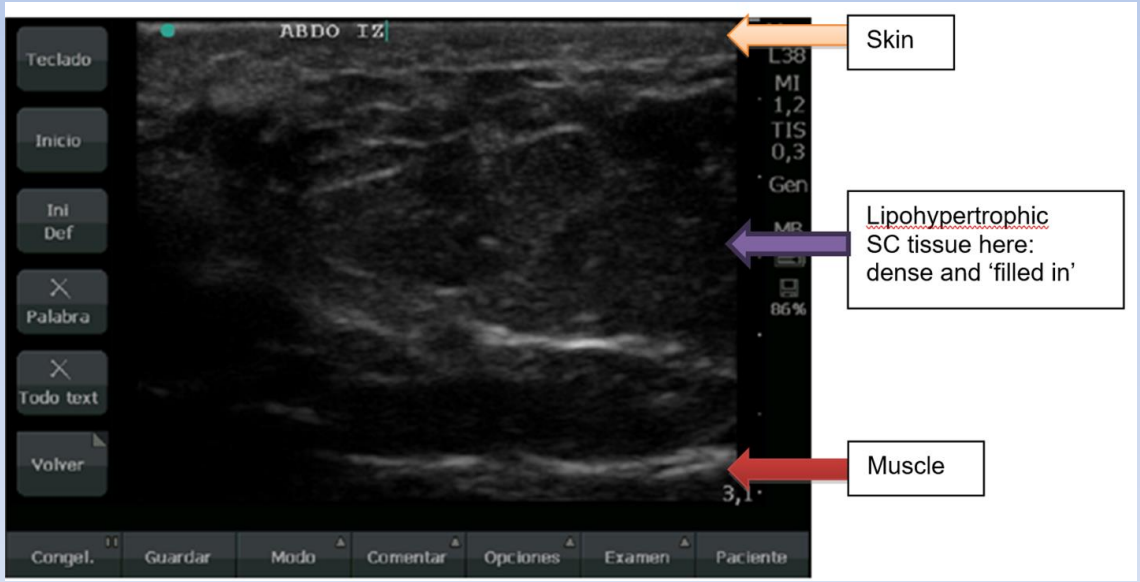
Prevalence and risk factors of lipohypertrophy in insulin-injecting patients with diabetes October 2013, Figure S1. M. Blanco, M.T. Hernández, K.W. Strauss, M. Amaya. https://doi.org/10.1016/j.diabet.2013.05.006

‘Echo-signature’ of Lipohypertrophy

Normal SC tissue



Lipohypertrophic SC tissue



Prevalence and risk factors of lipohypertrophy in insulin-injecting patients with diabetes October 2013, Figure S2. M. Blanco, M.T. Hernández, K.W. Strauss, M. Amaya. https://doi.org/10.1016/j.diabet.2013.05.006

Four most frequent types of lipohypertrophy



Type	Definition	Visibility	Palpable	Texture
A	Small nodule	Easily seen figure/ better with tangential light	Easily	Harsh-elastic
B	Large nodule	Clearly visible figure/ better with tangential light	Easily	Harsh-elastic
C	Flat plastron	Hardly visible	Not easily palpable/ better by pinching	Usually elastic
D	Flat nodule	Not visible	Difficult to identify, easier by deep palpation or pinching	Usually elastic

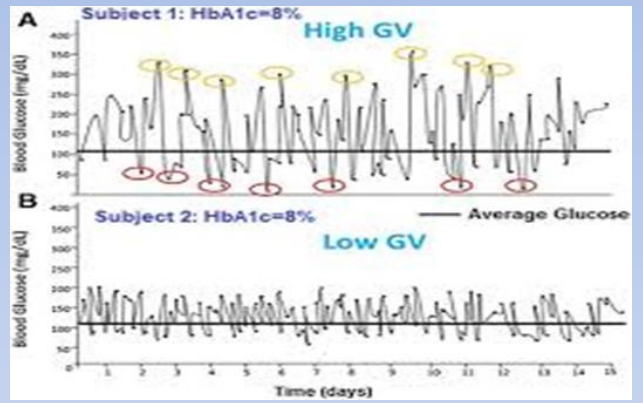
Gentile S, Strollo F, Guarino G, et al. Factors hindering correct identification of unapparent lipohypertrophy. J Diabetes Metab Disord Control. 2016;3(2):42-47. DOI: 10.15406/jdmdc.2016.03.00065

Consequences of lipohypertrophy

1. Injecting insulin into LH lesion

- Affects pharmacokinetics (absorption profile) of insulin
  - significant blunting of insulin absorption profiles
  - markedly increased variability when compared to injections into adjacent normal tissue

  (Famulla , and et al., 2016)

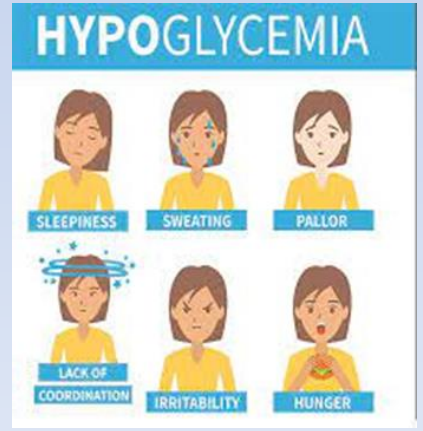


- ↑ risk of severe hypoglycaemia

  (Famulla, and et al., 2016; Gentile, and et al. ,2018; Johansson U-B, and et al.,2005)

- Unpredictable absorption of insulin

  (Famulla, and et al., 2016)



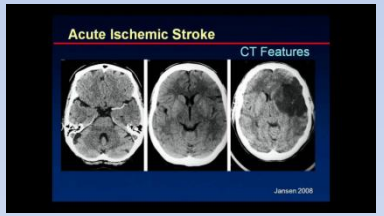
Consequences of lipohypertrophy

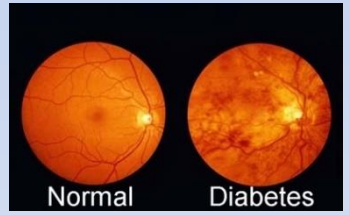
2. Pharmacokinetics alterations

- higher insulin consumption amount
- worsened glucose control
- higher HbA1c levels, and higher rates of unexplained hypoglycemia and glucose variability
  (Blanco, et al., 2013; Ji, et al., 2017, & Grassi, et al., 2014)









3. LH increases risk

- adverse clinical outcomes
- raises the cost of healthcare
  (Campinos, et al., 2017)

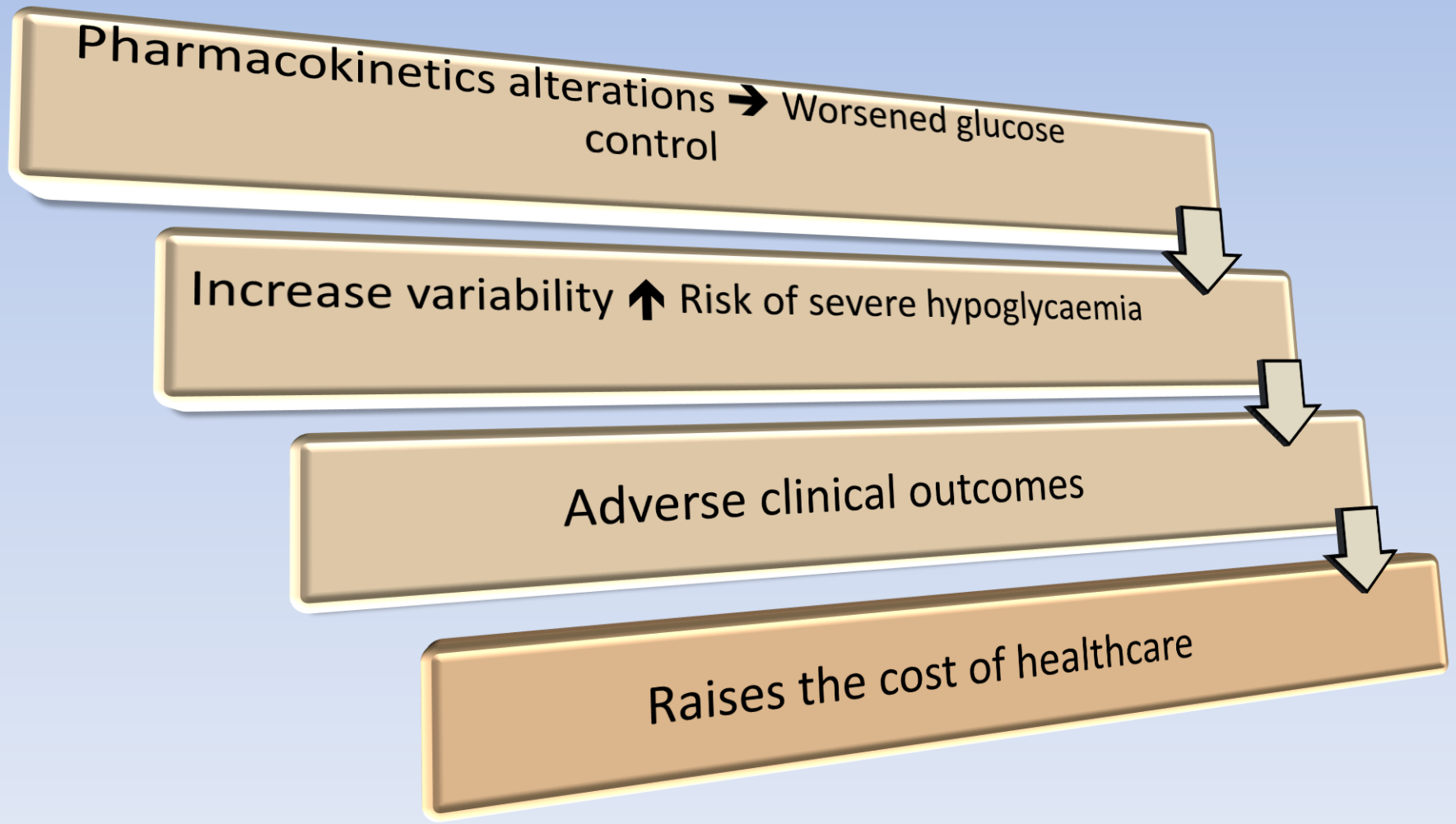




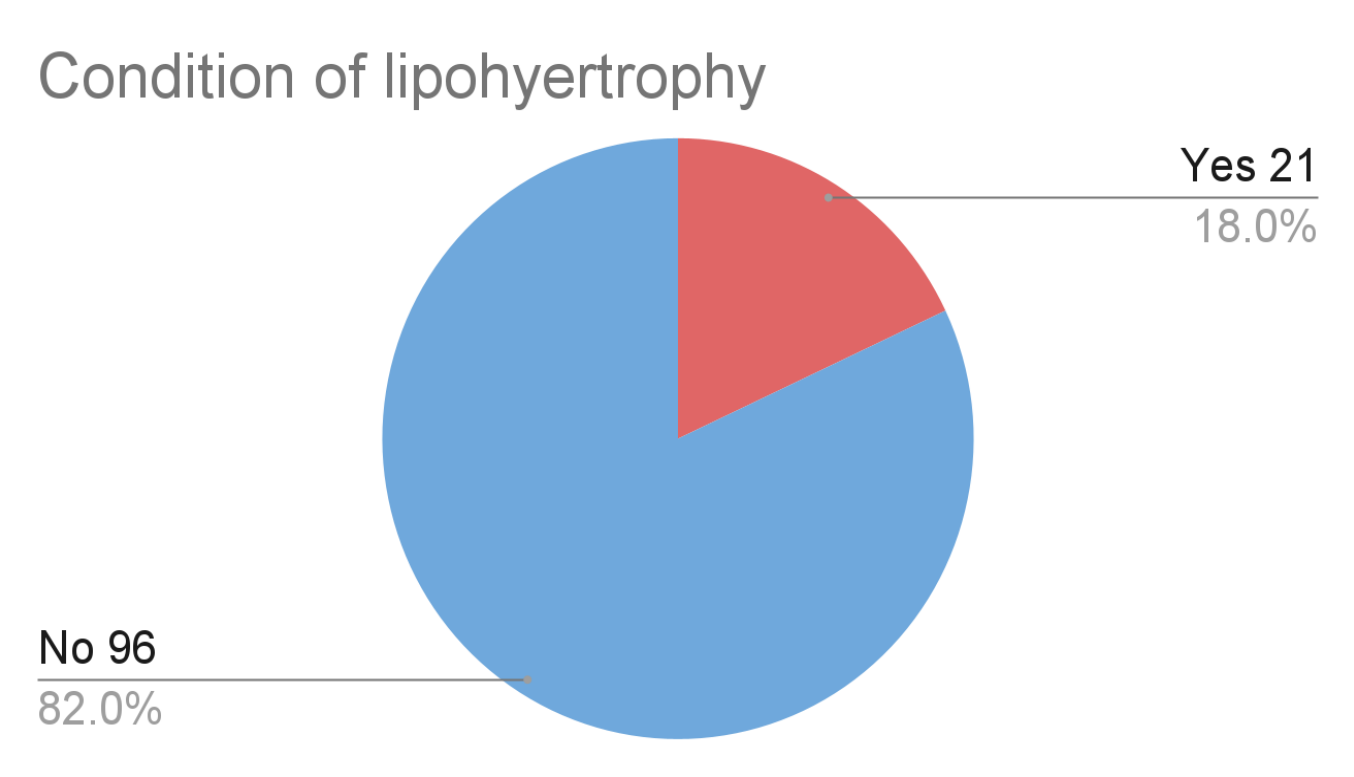




Consequences of lipohypertrophy

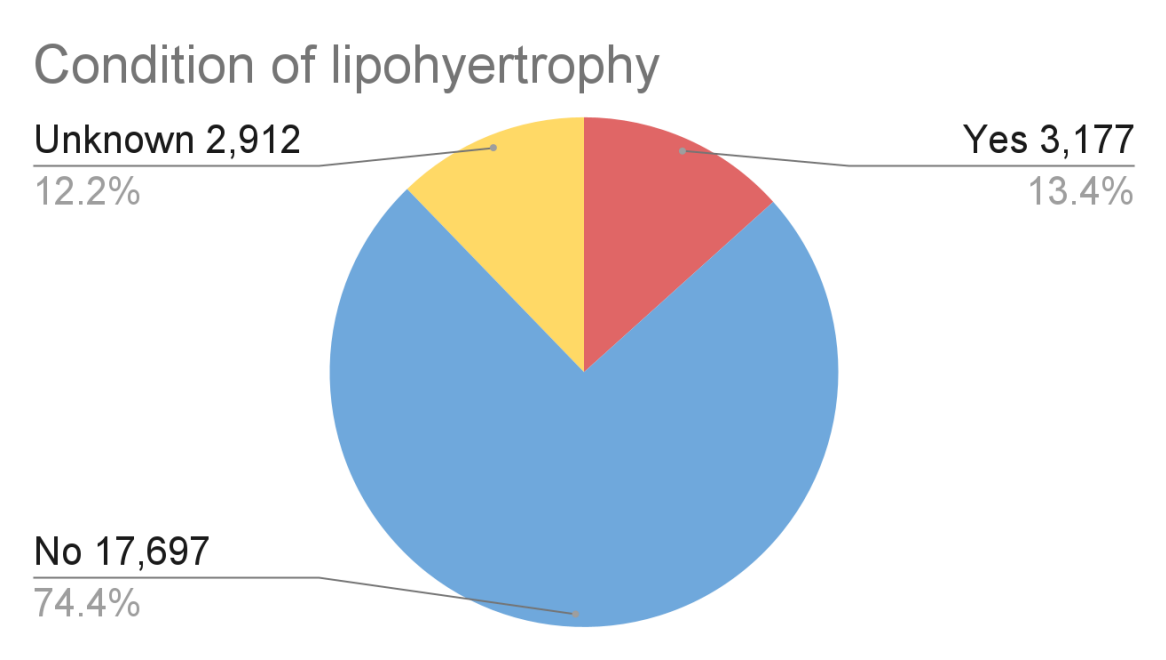


Local Prevalence of Lipohypertrophy



- **18.0 %** lipohypertrophy
- in 117 insulin users
- MRAM
- **PYNEH**
- 1/1/2021 to 28/2/2021

Local Prevalence of Lipohypertrophy

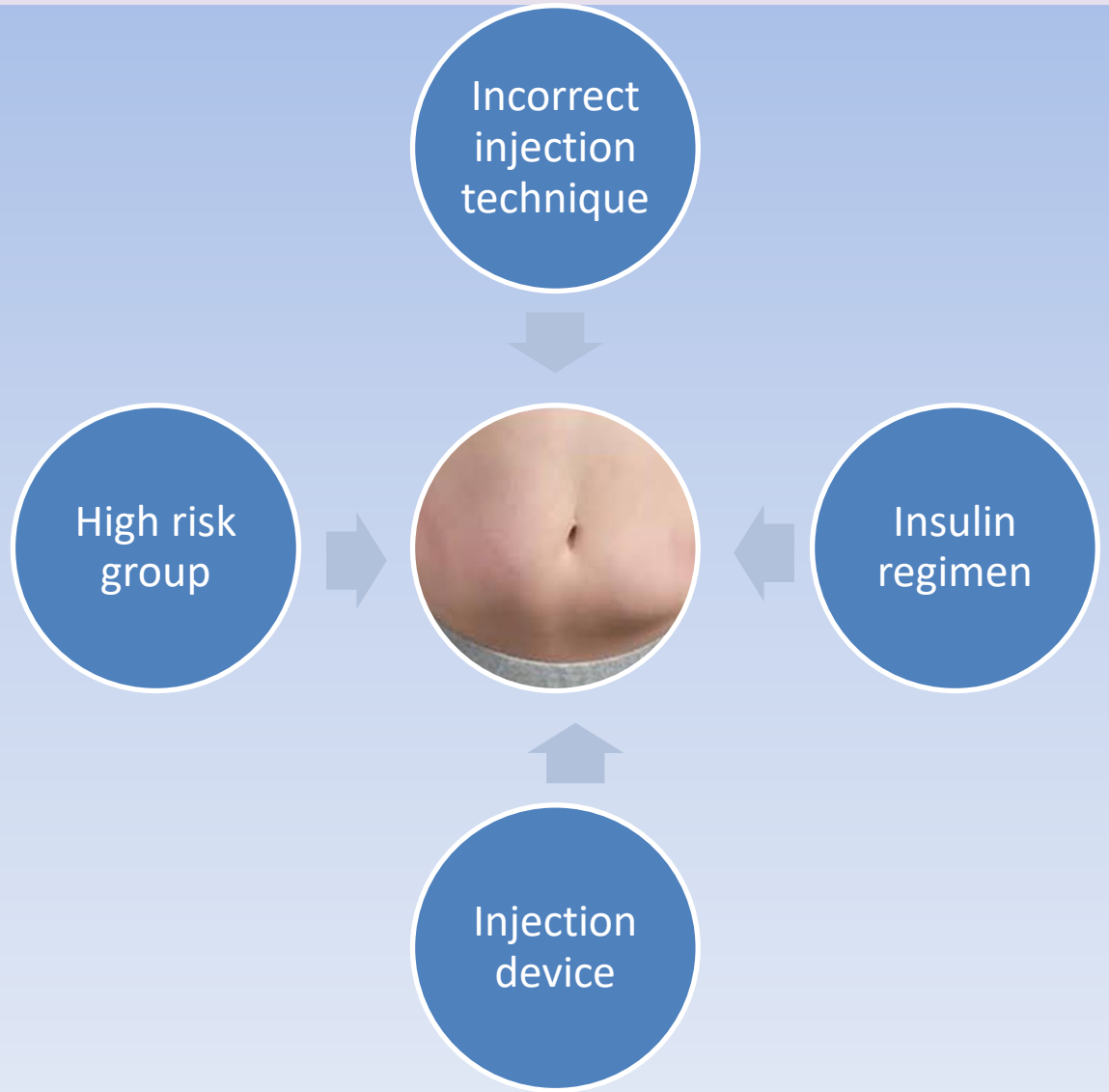


- **13.4 - 25.6%** lipohypertrophy
- 23,786 insulin users
- MRAM
- **Public hospitals and clinics**
- from 1/4/2020 to 31/3/2021

Global Prevalence of Lipohypertrophy

Detection method	Ultrasound (US) scanning	Observation and Palpation
Literature	Systematic review, included 16 articles from 3 database (Medline, Embase, Cinahl) from 2000-2017	Meta-analysis and Meta-regression, included 45 articles from 4 database (Pubmed, Embase, Scopus, Google Scholar) from inception to 2020
Number of Participants	1722 patients (T1DM and T2DM)	26865 patients (T1DM and T2DM)
Prevalence of lipohypertrophy	**Median: 56.6%** (Abu Ghazaleh et al., 2018) **<u>The lowest:</u> China: 14.5% (**included 509 patients; no data about the assessors) (Wang et al., 2014) **<u>The highest:</u> Romania: 88%** (included 40 patients; no data about the assessors) (Perciun 2010)	**Overall: 41.8%** (95% CI: 35.9% to 47.6%) **<u>Region-wise analysis</u>**: **Europe: 44.6%** (95% CI 37.5% to 51.8%) **Asia: 41.3%** (95% CI 27.2% to 55.3%) **Africa: 34.8%** (95% CI 16.9% to 52.8%) (Wang, Zhang, Liu & Chen, 2021)

Lipohypertrophy Risk factors



1. Incorrect Insulin Injection Technique

- Lack of proper injection site rotation
- Needle reuse
- Cold insulin injection (Gentile et al., 2021)
- Drop leakage after injection

  (From the questionnaire focused on injection technique)





Gentile S, Strollo F, Guarino G, et al. Factors hindering correct identification of unapparent lipohypertrophy. J Diabetes Metab Disord Control. 2016;3(2):42-47. DOI: 10.15406/jdmdc.2016.03.00065

Why patients continue to inject insulin into LH?

- Absence of pain
- “Ergonomic-like” habits
- Not trained on how to inject insulin





2. Insulin regimen

- Higher daily insulin dose
- Longer insulin treatment duration
- Multiple injections
- Use of human insulin

(Thewjitcharoen et al., 2020)

3. Injection device

- Longer pen needle length (8mm)

- Larger pen needle gauge (Ng, Chui & Tiu, 2015)



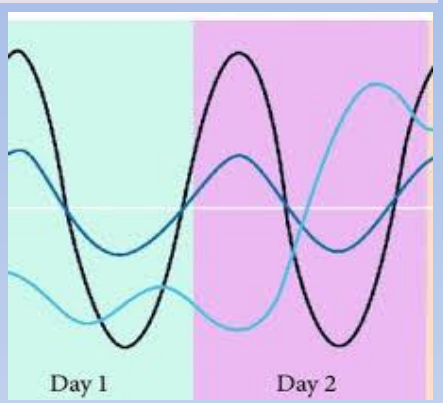




4. High risk group for LH

- Frequent with unexplained hypoglycemia
- Poor DM control with HbA1c > 9%
- Large glycemic variability
- Longer DM duration
- Long standing Type 1 DM (Thewjitcharoen et al., 2020)
- Older patients > 65 years old
  - Lower thickness, vascularity and elasticity and a more prominent fibrous texture (all affect tissue distensibility)
  - Less able to accommodate large volume of insulin containing fluid
- Living alone and being retired were associated with LH
  - Depression and poor self-care adversely affected insulin injection behaviour (Gentile et al., 2020)
- Body Mass Index (BMI)
  - Obese with BMI 25 or higher (Gentile et al., 2020 ; Surucu & Arsalan, 2018; and Al Hayek et al., 2016)
  - Low BMI in T1DM (Barola et al., 2016)





Subclinical lipohypertrophy

Higher BMI	OR = 1.44	95%CI: 1.15-1.81	P = 0.002
Incorrect rotation of sites	OR = 3.11	95%CI: 1.02-9.47	P = 0.046
Insulin needle reusage for more than four times	OR = 10.00	95%CI: 3.23-31.02	P = 0.000
Type 1 diabetes	OR = 6.33	95%CI: 1.32-30.47	P = 0.021
Nonoptimal glycemic control	OR = 9.97	95% CI: 3.46-28.75	P = 0.000

Luo D, Shi Y, Zhu M, Wang H, Yan D, Yu J, Ji J, Liu X, Fan B, Xu Y, Zhang M, He W, Xu J, Yang T. Subclinical lipohypertrophy--Easily ignored complications of insulin therapy. J Diabetes Complications. 2021 Mar;35(3):107806. doi: 10.1016/j.jdiacomp.2020.107806. Epub 2020 Nov 26. PMID: 33280982.

Findings from our literature review (1)

- **Clinical Gap**
  - inadequate training (Gentile, et al., 2021)
  - Use only visual examination (Misnikova, et al., 2017)

- **When to assess lipohypertrophy?**
  - Insulin initiation (Misnikova, et al., 2017)
  - Yearly (Gentile, et al., 2021)
  - Intensive nurse training on proper injection techniques followed by patient education (Smith, et al., 2017)

Findings from literature review (2)

- **How to prevent lipohypertrophy?**
  - 4mm pen needles
  - Correct rotation method
  - Move injection to non-LH areas
  - Stop needle reuse
  - Stop inject to LH area (Misnikova, et al., 2017)
- **Education format**
  - 60 mins education session, then individual training session (Gentile, et al., 2021)
  - Individual training session address real lives injection problems (Gentile, et al., 2021)
  - Intensive injection technique education (Campinos, et al, 2017)
  - Proper injection technique education (Chen, et al., 2021)
- **Education resources**
  - Injection technique leaflets
  - LH models “look and feel” teaching (Gentile, et al., 2021)

Start rotating, keep rotating

1 Choose an area eg. Abdomen



2 Select injection zone



3 Use arotation grid to help
For the first few times



4 Inject 1 finger's width away
From the last injection

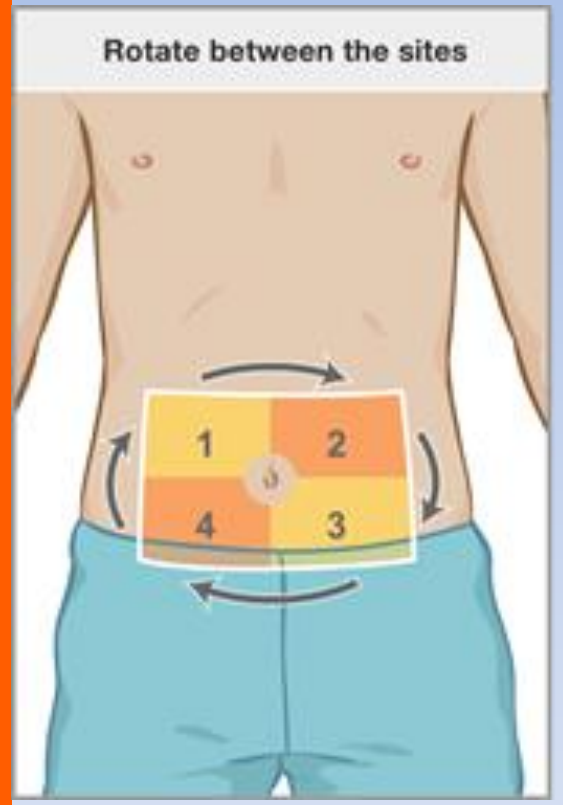


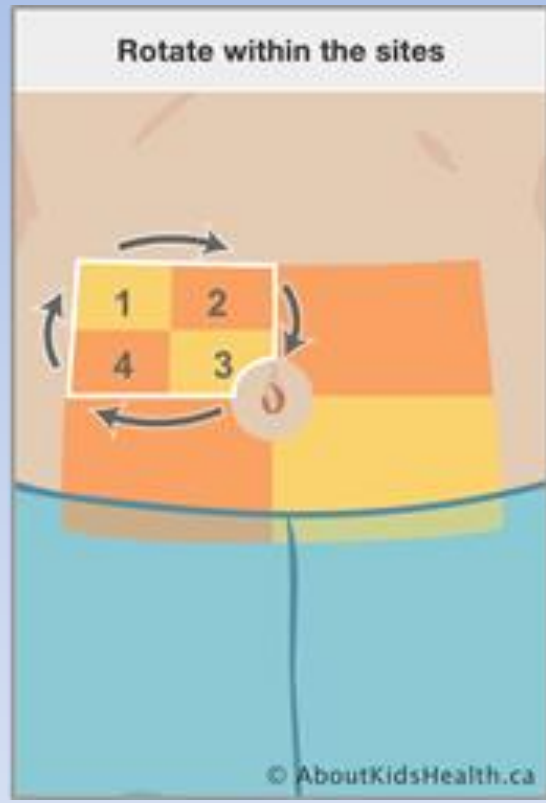
5 Complete zone move on to next



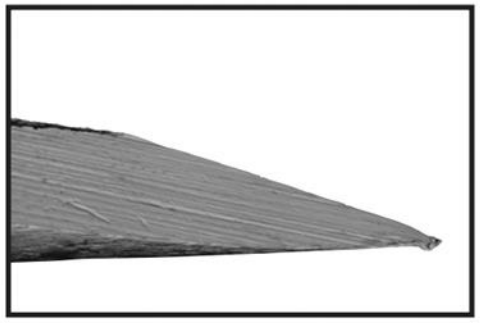
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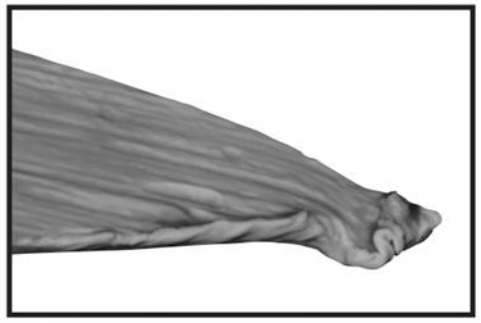




Prevention of Lipohypertrophy: Use a new needle

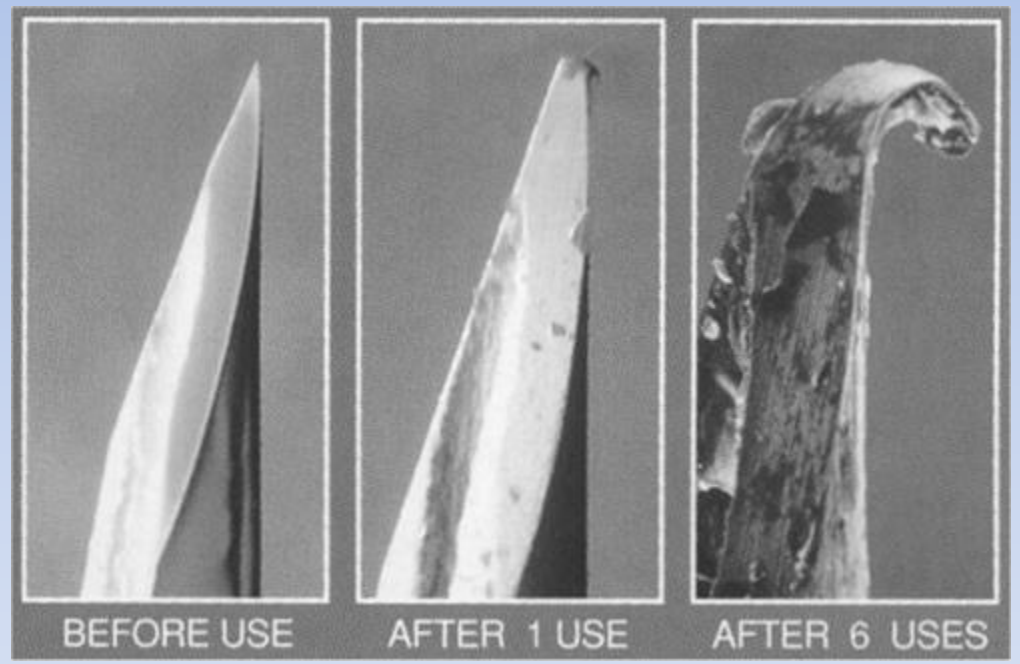


Used needle magnified 370 times



Same used needle magnified 2000 times

* Photographs from Dieter Look and Kenneth Strauss study:
"Nadeln mehrfach verwenden?" Diabetes Journal 1998, 10: S. 31-34.



Proper insulin injection technique

Hospital Authority

Insulin Injection Assessment Form (Insulin Pen) for Patient / Carer

Record Method
1) Attained item : ✓
2) Not attained item : ×
3) Not Applicable : NA

Patient's name: _____
Hosp/SOP/CNS No: _____
Or Patient Label

Performed by Patient / Carer (delete inappropriate)

Pen Needle ☐ 4mm ☐ 5mm ☐ 6mm

© Critical Point for Assessment

	Assessment item	Date of teaching	Date of Assessment						Remarks
Before injection	1. Clean hands								
	2. Prepare materials: insulin pen, ± penfill insulin, pen needle and alcohol swab								
	3. Ensure the correct name of insulin, before expiry date and no abnormalities such as clumps or discolouration								
	4. State the insulin storage method								
	5. © Tip cloudy insulin up and down to 180 degrees at least 20 cycles								
	6. Clean the rubber membrane of the penfill insulin by alcohol swab								
	7. Screw on a new pen needle								
	8. Priming of insulin pen until a drop of insulin dripping out								
	8.1 Dial 1 to 2 units of insulin and press the dose button for testing								
	8.2 Repeat 8.1 until a drop of insulin dripping out								
	9. © Dial to the prescribed dose of insulin								
Injection procedure	10. © Assess and confirm a suitable injection point (If necessary, pinch up a skin fold by using 2 fingers)								
	11. Clean skin and wait till dry								
	12. Insert the pen needle completely into skin at 90°								
	13. Press the dose button until the display window shown "0"								
	14. Keep the pen needle in-situ for at least 10 seconds								
	15. Withdraw the needle at the same angle. Press the injection point gently and avoid massage								
	16. Check the display window shown "0"								
After injection	17. Recap the needle with the outer cap and unscrew it from the pen								
	18. Discard the used needle into a container with lid								
	19. Store in-use insulin pen at room temperature and avoid direct sunlight								
Change new penfill insulin	20. Confirm the need to change a new penfill insulin								
	21. Remove the used penfill insulin								
	22. Replace a new penfill insulin into the cartridge holder and lock the cartridge holder on the insulin pen tightly								
	Nurse Signature:								

Hospital Authority

Insulin Injection Assessment Form (Insulin Syringe) for Patient / Carer

Record Method
1) Attained item : ✓
2) Not attained item : ×
3) Not Applicable : NA

Patient's name: _____
Hosp/SOP/CNS No: _____
Or Patient Label

Performed by Patient / Carer (delete inappropriate)

© critical point for assessment

	Assessment item	Date of teaching	Date of assessment						Remarks
Before injection	1. Understand insulin syringe and its markings								
	2. Clean hands								
	3. Prepare materials: insulin vial, insulin syringe and alcohol swab								
	4. Ensure the correct name of insulin, before expiry date and no abnormalities such as clumps or discolouration								
	5. State the insulin storage method								
	6. Draw insulin								
	6.1 © Mix cloudy insulin well by gently rolling or inverting the insulin vial								
	6.2 Clean the rubber membrane of insulin vial by alcohol swab								
	6.3 Draw the required units of air and inject all air into the vial								
	6.4 Turn the vial upside down, draw out a few units of insulin and push back to the vial, repeat 2 to 3 times to expel air								
	6.5 © Draw the required units of insulin and confirm correct dose of insulin								
Injection procedure	7. © Assess and confirm a suitable injection point. Pinch up a skin fold by using 2 fingers								
	8. Clean skin and wait till dry								
	9. Insert the needle into skin at 45°to 90°								
	10. Push the plunger to inject insulin into skin								
	11. Release skin and take out the needle at the same angle								
	12. Press the injection point and avoid massage								
After injection	13. Discard the used insulin syringe into a container with lid								
	14. Store in-use insulin vial at room temperature and avoid direct sunlight								
	Nurse Signature:								

Assessment of lipohypertrophy

Environmental preparation

- **Warm** (FIT UK, 2020)
- Use direct & **tangential light** against a dark background

  (Gentile et al., 2016)
- Light shine at 30-45 degrees

  (FIT UK, 2020)

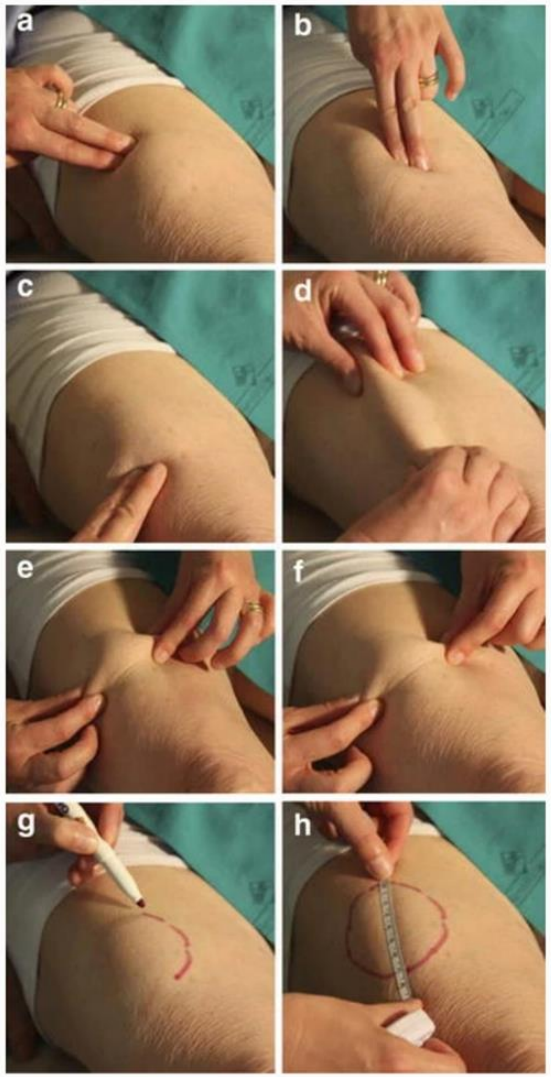
Patient Positioning

- **Supine** position with pillow with knees bent and arms folded over chest (FIT UK, 2020) (Frid et al., 2016)
- Lie on alternate sides to examine the buttock area (BD, 2018)
- Frail, sit with knees bent and arms relaxed in thighs

  (FIT UK, 2020)
- Stand up & let their arms hang by their sides for examining abdomen & buttocks (BD, 2018)
- From upright to the supine position or vice-versa

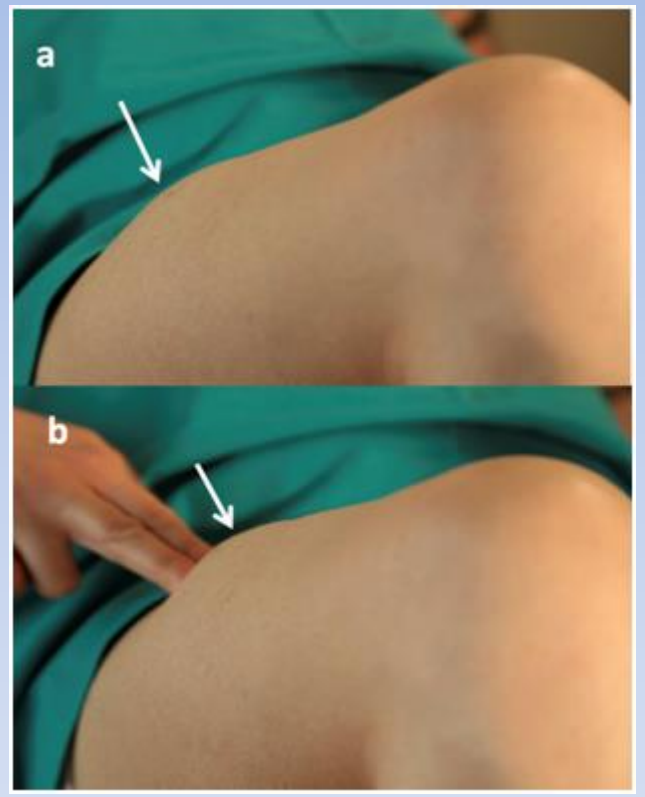
  (Gentile et al., 2019)

Palpation technique



- **Lubricant** (Gentile et al., 2020)
- Slow **circular** & vertical finger tip movements (Gentile et al., 2016)
- Be gentle at the beginning & **increase finger pressure** gradually (Gentile et al., 2016)
- Perform the **pinch maneuver** when recognizing a harder skin (Gentile et al., 2016)
- **Mark** the exact position of the lipohypertrophy with marker pen (FIT UK, 2020)

Palpation maneuvers



Tangential light (panel a)
pressure exerted close to the lesion (panel b)



Abdominal flat lipohypertrophy area

Gentile S, Strollo F, Guarino G, et al. Factors hindering correct identification of unapparent lipohypertrophy. J Diabetes Metab Disord Control. 2016;3(2):42-47. DOI: 10.15406/jdmdc.2016.03.00065

Checklist for Assessment of lipohypertrophy

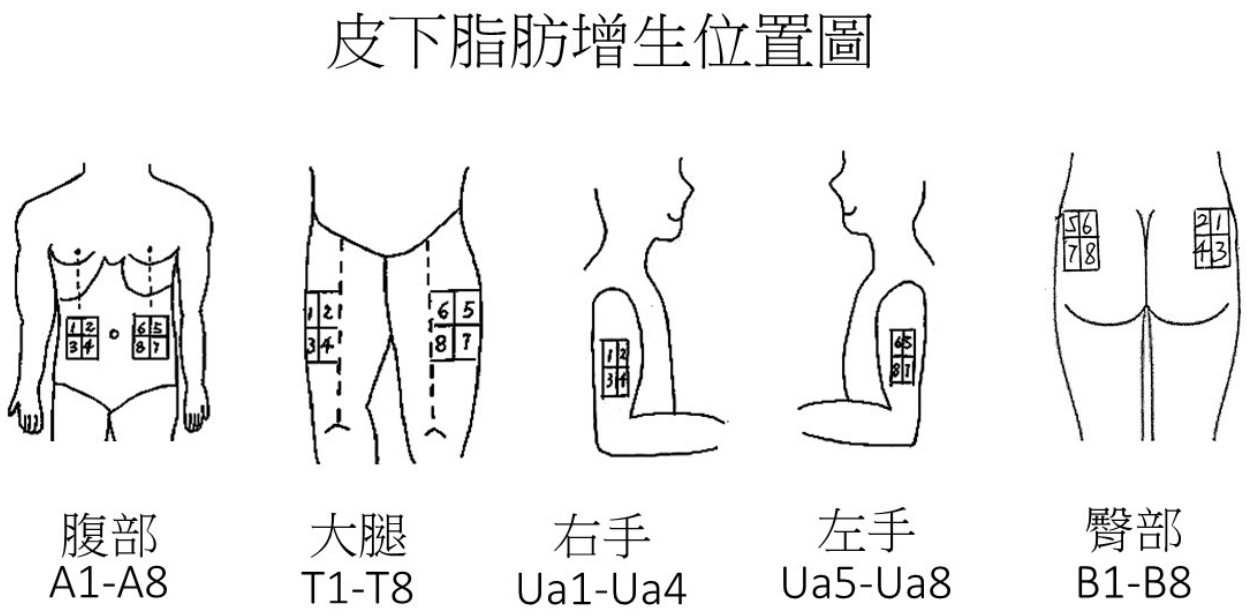
Assessment of lipohypertrophy
1. *Environmental preparation*
a. Ensure the room is warm to prevent chilling (prevents shivering and muscle tension)
b. Using direct and tangential light against a dark background for inspection
c. Light should be shined onto skin surfaces at an angle of 30-45 degrees
2. *Positioning of patient*
a. Ideally in a supine position with 1 supporting pillow on examination bed (to relax abdominal muscles) with knees bent (to relax thigh quadriceps muscles) and arms folded over chest (to relax arm muscles)
b. To examine the buttock area, ask the patient to lie on alternate sides and flex their knees towards, their chest to relax their gluteal muscles, examining the upper facing buttock area
c. If the patient is frail, sit with knees bent and arms relaxed in thighs
d. In case without examination bed, ask the patient to stand up and let their arms hang by their sides for examining abdomen and buttocks. For examining the thighs, ask the patient to sit upright in a chair with their hands resting in their knees and their legs at right angles to the floor
e. Change from upright to the supine position or vice-versa during assessment
f. Soft protruding lipohypertrophy is less visible under supine position
g. For weight decrease group (10-20% weight decrease), lipohypertrophy is more correctly identified in upright position than in supine position

3. Palpation technique.
a. Warm your hands before touching patient.
b. Apply lubricant on assessment site.
c. Start with gentle slow circular and vertical fingertip movements and then followed by gradual increasing finger pressure with repeated horizontal attempts on the same spot.
d. Perform the pinch maneuver when recognizing a harder skin.
4. Documentation.
a. Mark the exact position of the lipohypertrophy with marker pen so that patient can avoid injecting into it.
b. Document the size and location (refer to the diagram 1) of lipohypertrophy (e.g. the size of lipohypertrophy is 8mmx12mm, the site is on abdomen A1, can write as A1, 8x12).

Microsoft Word Document

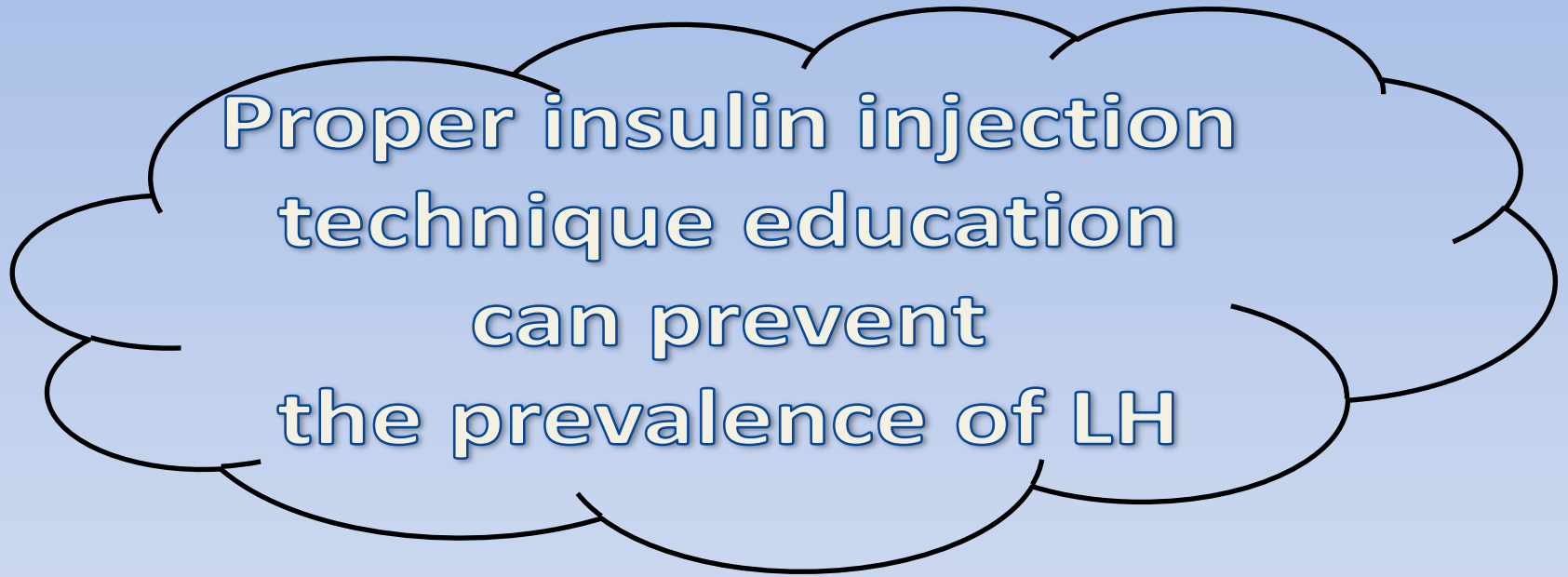


Documentation of Lipohypertrophy



Example:
The size of lipohypertrophy is 8mmx12mm, the site is on abdomen A1, can write as
A1, 8x12

Take Home message



- A correct injection technique is essential to
  - avoid lipohypertrophy in people with diabetes
  - ensure fully predictable insulin effect & good metabolic control
  - prevent he risk of repeated hypo- and hyper-glycaemic episodes

- Flat, small and arm-localized LH lesions are most often missed

References

- Abu Ghazaleh, H., Hashem, R., Forbes, A., Dilwayo, T. R., Duaso, M., Sturt, J., Halson-Brown, S., & Mulnier, H. (2018). A Systematic Review of Ultrasound-Detected Lipohypertrophy in Insulin-Exposed People with Diabetes. Diabetes therapy : research, treatment and education of diabetes and related disorders, 9(5), 1741–1756. https://doi.org/10.1007/s13300-018-0472-7
- Al Hayek, A.A., Robert, A.A., Braham, R.B. et al. Frequency of Lipohypertrophy and Associated Risk Factors in Young Patients with Type 1 Diabetes: A Cross-Sectional Study. DiabetesTher 7, 259–267(2016). https://doi.org/10.1007/s13300-016-0161-3
- Barola, A., Tiwari, P., Bhansali, A., Grover, S., & Dayal, D. (2018). Insulin-Related Lipohypertrophy: Lipogenic Action or Tissue Trauma? Frontiers in Endocrinology. 9 (638). doi: 10.3389/fendo.2018.00638
- BD. (2018). Detecting, treating & preventing lipohypertrophy.
- Blanco M, Hernández MT, Strauss KW, Amaya M: Prevalence and risk factors of lipohypertrophy in insulin-injecting patients with diabetes. Diabetes Metab 2013;39:445–453. https://doi.org/10.1016/j.diabet.2013.05.006
- Campinos, C., Le Floch, J. P., Petit, C., Penfornis, A., Winiszewski, P., Bordier, L., Lepage, M., Fermon, C., Louis, J., Almain, C., Morel, D., Hirsch, L., & Strauss, K. W. (2017). An Effective Intervention for Diabetic Lipohypertrophy: Results of a Randomized, Controlled, Prospective Multicenter Study in France. Diabetes technology & therapeutics, 19(11), 623–632. https://doi.org/10.1089/dia.2017.0165
- Chen, L., Xing, Q., Li, J., Zhou, J., Yuan, Y., Wan, Y., Pflug, B. K., Strauss, K. W., & Hirsch, L. J. (2021). Injection Technique Education in Patients with Diabetes Injecting Insulin into Areas of Lipohypertrophy: A Randomized Controlled Trial. Diabetes therapy : research, treatment and education of diabetes and related disorders, 12(3), 813–826. https://doi.org/10.1007/s13300-021-01013-1

- Famulla S, Hövelmann U, Fische A, et al.: Insulin injection into lipohypertrophic tissue: blunted and more variable insulin absorption and action and impaired postprandial glucose control. Diabetes Care 2016;39:1486-92. https://doi.org/10.2337/dc16-0610
- FIT UK Forum for Injection Technique UK. The UK injection and infusion technique recommendations,4thed.2016. http://www.fit4diabetes.com/files/4514/7946/3482/FIT_UK_Recommendations_4th_Edition.pdf.
- Frid, A. H., Kreugel, G., Grassi, G., Halimi, S., Hicks, D., Hirsch, L. J., Smith, M. J., Wellhoener, R., Bode, B. W., Hirsch, I. B., Kalra, S., Ji, L., & Strauss, K. W. (2016). New Insulin Delivery Recommendations. Mayo Clinic Proceedings, 91(9), 1231-1255. https://doi.org/10.1016/j.mayocp.2016.06.010
- Fujikura, J., Fujimoto, M., Yasue, S., Noguchi, M., Masuzaki, H., Hosoda, K., Tachibana, T., Sugihara, H., & Nakao, K. (2005). Insulin-induced lipohypertrophy: report of a case with histopathology. Endocrine journal, 52 5, 623-8 .
- Gentile S, et al. Factors hindering correct identification of unapparent lipohypertrophy. JDiabetesMetabDisordControl.2016;3(2):00065.DOI: 10.15406/jdmdc.2016.03.00065
- Gentile S, et al. Skin complications of insulin injections: a case presentation and a possible explanation of hypoglycaemia. Diabetes Res Clin Pract. 2018;138:284–7. https://doi.org/10.1016/j.diabres.2018.02.005
- Gentile S, Guarino G, Della Corte T, Marino G, Fusco A, Corigliano G, Colarusso S, Piscopo M, Improta MR, Corigliano M, Martedi E, Oliva D, Russo V, Simonetti R, Satta E, Romano C, Vaia S, Strollo F; AMD-OSDI Study Group on Injection Techniques; Nefrocenter Network and Nyx Start-up Study Group. Lipohypertrophy in Elderly Insulin-Treated Patients With Type 2 Diabetes. Diabetes Ther. 2021 Jan;12(1):107-119. doi: 10.1007/s13300-020-00954-3. Epub 2020 Nov 21. PMID: 33219928; PMCID: PMC7843727.
- Gentile S, Guarino G, Della Corte T, Marino G, Satta E, Romano C, Alfrone C, Lmberti C, Strollo F; AMD-OSDI Study Group. Bruising: A Neglected, Though Patient-Relevant Complication of Insulin Injections Coming to Light from a Real-Life Nationwide Survey. Diabetes Ther. 2021 Apr;12(4):1143-1157. doi: 10.1007/s13300-021-01026-w. Epub 2021 Mar 9. PMID: 33687646; PMCID: PMC7994491.

- Gentile, S., Guarino, G., Corte, T. D., Marino, G., Fusco, A., Corigliano, G., Colarusso, S., Piscopo, M., Improta, M. R., Corigliano, M., Martedì, E., Oliva, D., Russo, V., Simonetti, R., Satta, E., Romano, C., Alfarone, C., Vetrano, A., Martino, C., Lamberti, C., AMD-OSDI Study Group on Injection Techniques and Nefrocenter Research & Nyx Start-up Study Group (2020). Insulin-Induced Skin Lipohypertrophy in Type 2 Diabetes: a Multicenter Regional Survey in Southern Italy. Diabetes therapy : research, treatment and education of diabetes and related disorders, 11(9), 2001–2017. https://doi.org/10.1007/s13300-020-00876-0
- Gentile, S., Guarino, G., Della Corte, T. Marino G, Satta E, Pasquarella M, Romano C, Alfrone C, Strollo F; AMD-OSDI Study Group on Injection Technique, Nefrocenter Research and Nyx Start-Up. Role of Structured Education in Reducing Lypodistrophy and its Metabolic Complications in Insulin-Treated People with Type 2 Diabetes: A Randomized Multicenter Case–Control Study. Diabetes Ther 12, 1379–1398 (2021). https://doi.org/10.1007/s13300-021-01006-0
- Gentile, S., Guarino, G., Giancaterini, A., Guida, P., & Strollo, F. (2016). A suitable palpation technique allows to identify skin lipohypertrophic lesions in insulin-treated people with diabetes. SpringerPlus, 5(1). https://doi.org/10.1186/s40064-016-1978-y
- Gentile, S., Strollo, F., Guarino, G., Brancario, C., Corigliano, M., Cozzolino, G., Improta, M., Fasolino, A., Lamberti, C., Lapice, M., Martino, C., Oliva, D., Raffaele, A., Selleri, A., Simonetti, R., Stile, A., Vecchiato, A., Vetrano, A., Volpe, P., . . . Vietsi, F. (2019). Why are so huge differences reported in the occurrence rate of skin lipohypertrophy? Does it depend on method defects or on lack of interest? Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 13(1), 682–686. https://doi.org/10.1016/j.dsx.2018.11.042
- Grassi G, Scuntero P, Trepiccioni R, et al.: Optimizing insulin injection technique and its effect on blood glucose control. J Clin Translat Endocrinol 2014;1:145–150. https://doi.org/10.1016/j.jcte.2014.07.006
- Hauner H, Stockamp B, Haastert B. Prevalence of lipohypertrophy in insulin-treated diabetic patients and predisposing factors. Exp Clin Endocrinol Diabetes. 1996;104(2):106–10.
- Ji L, Li Q, Wei G: Lipohypertrophy—prevalence, risk factors and clinical characteristics of insulin-requiring patients in China. Diabetes Technol Ther 2017;19:61–67. https://doi.org/10.1089/dia.2016.0334
- Johansson U-B, et al. Impaired absorption of insulin aspart from lipohypertrophic injection sites. Diabetes Care. 2005;28(8):2025–7

- Misnikova, I. V., Gubkina, V. A., Lakeeva, T. S., & Dreval, A. V. (2017). A Randomized Controlled Trial to Assess the Impact of Proper Insulin Injection Technique Training on Glycemic Control. Diabetes therapy : research, treatment and education of diabetes and related disorders, 8(6), 1309–1318. https://doi.org/10.1007/s13300-017-0315-y
- Ng, C.M., Chui, O.L. & Tiu, S. C. (2015). 'Cleft sign' of severe Lipohypertrophy. Hong Kong Med J 2015; 21:475.e3-4. DOI: 10.12809/hkmj154528
- Perciun R. Ultrasonographic aspect of subcutaneous tissue dystrophies as a result of insulin injections. Med Ultrasonogr. 2010;12(2): 104-9.
- Smith, M., Clapham, L., & Strauss, K. (2017). UK lipohypertrophy interventional study. Diabetes research and clinical practice, 126, 248–253. https://doi.org/10.1016/j.diabres.2017.01.020
- Surucu, H.A. & Arslan, H.O. (2018). Lipohypertrophy in Individuals with Type 2 Diabetes: Prevalence and Risk Factors. Journal of Caring Sciences. 7(2): 67-74. doi: 10.15171/jcs.2018.011
- The Forum for Injection Techniques (FIT). (2020, December). www.Fit4diabetes.Com.http://www.fit4diabetes.com
- Thewjitcharoen, Y., Prasartkaew, H., Tongsumrit, P., Wongjom, S., Boonchoo, C., Butadej, S., Nakasatien, S. Karndumri, K., Veerasomboonsin, V., Krittiyawong, S. & Himathongkam, T. (2020). Prevalence, Risk factors, and Clinical Characteristics of Lipodystrophy in Insulin-Treated Patients with Diabetes: An Old Problem in a New Era of Modern Insulin. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy:13, 4609-4620. doi.org/102147/DMSO.S282926
- Wang K, Zhang S, Liu C, Chen Y. A meta-analysis and meta-regression on the prevalence of lipohypertrophy in diabetic patients on insulin therapy. Therapie. 2021 Apr 20:S0040-5957(21)00098-6. doi: 10.1016/j.therap.2021.04.002. Epub ahead of print. PMID: 33958198.
- Wang W, Guo X, Shen G. Skin and subcutaneous layer thickness and prevalence of lipodystrophy at sites used for insulin injections in Chinese diabetic patients. Diabetes. 2014;63:A603.


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